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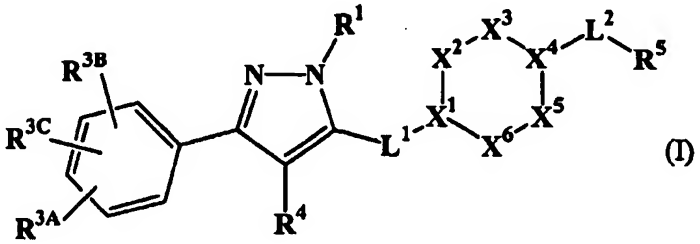
(54) Title: PYRAZOLE-DERIVATIVES AS P38 KINASE INHIBITORS



(I)

(57) Abstract: This invention is directed generally to pyrazoles that, *inter alia*, inhibit p38 kinase, TNF, and/or cyclooxygenase-2 activity. Such pyrazoles include compounds generally corresponding in structure to the following formula (I), wherein L^1, L^2, X^1, X^2, X^3, X^4, X^5, X^6, R^1, R^{3A}, R^{3B}, R^{3C}, R^4, and R^5 are as defined in this specification. The pyrazoles further include tautomers of such compounds, as well as salts of such compounds and tautomers. This invention also is directed to compositions of such pyrazoles, intermediates for the syntheses of such pyrazoles, methods for making such pyrazoles, and methods for treating (including preventing) conditions (particularly pathological conditions) associated with p38 kinase, TNF, and/or cyclooxygenase-2 activity.

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PYRAZOLE-DERIVATIVES AS P38 KINASE INHIBITORS

FIELD OF THE INVENTION

[1] This invention is directed to pyrazole compounds (including tautomers of the compounds, and salts of the compounds and tautomers) that, *inter alia,* generally tend to inhibit p38 kinase (particularly p38α kinase), TNF (particularly TNF-α), and/or cyclooxygenase (particularly cyclooxygenase-2 or "COX-2") activity. This invention also is directed to compositions of such pyrazoles (particularly pharmaceutical compositions), intermediates for the syntheses of such pyrazoles, methods for making such pyrazoles, and methods for treating (including preventing) conditions (typically pathological conditions) associated with p38 kinase activity, TNF activity, and/or cyclooxygenase-2 activity.

BACKGROUND OF THE INVENTION

[2] Mitogen-activated protein kinases (MAP) constitute a family of proline-directed serine/threonine kinases that activate their substrates by dual phosphorylation. The kinases are activated by a variety of signals, including nutritional and osmotic stress, UV light, growth factors, endotoxin, and inflammatory cytokines. The p38 MAP kinase group is a MAP family of various isoforms, including p38α, p38β, and p38γ. These kinases are responsible for phosphorylating and activating transcription factors (*e.g.*, ATF2, CHOP, and MEF2C), as well as other kinases (*e.g.*, MAPKAP-2 and MAPKAP-3). The p38 isoforms are activated by bacterial lipopolysaccharide, physical and chemical stress, and pro-inflammatory cytokines, including tumor necrosis factor ("TNF") and interleukin-1 ("IL-1"). The products of the p38 phosphorylation mediate the production of inflammatory cytokines, including TNF, IL-1, and cyclooxygenase-2.

[3] It is believed that p38α kinase can cause or contribute to the effects of, for example, inflammation generally; arthritis; neuroinflammation; pain; fever; pulmonary disorders; cardiovascular diseases; cardiomyopathy; stroke; ischemia; reperfusion injury; renal reperfusion injury; brain edema; neurotrauma and brain trauma; neurodegenerative disorders; central nervous system disorders; liver disease and nephritis; gastrointestinal conditions; ulcerative diseases; ophthalmic diseases; ophthalmological conditions; glaucoma; acute injury to the eye tissue and ocular traumas; diabetes; diabetic

nephropathy; skin-related conditions; viral and bacterial infections; myalgias due to infection; influenza; endotoxic shock; toxic shock syndrome; autoimmune disease; bone resorption diseases; multiple sclerosis; disorders of the female reproductive system; pathological (but non-malignant) conditions, such as hemaginomas, angiofibroma of the nasopharynx, and avascular necrosis of bone; benign and malignant tumors/neoplasia including cancer; leukemia; lymphoma; systemic lupus erthrematosis (SLE); angiogenesis including neoplasia; and metastasis.

[4] TNF is a cytokine produced primarily by activated monocytes and macrophages. Excessive or unregulated TNF production (particularly TNF-α) has been implicated in mediating a number of diseases. It is believed, for example, that TNF can cause or contribute to the effects of inflammation (*e.g.*, rheumatoid arthritis and inflammatory bowel disease), asthma, autoimmune disease, graft rejection, multiple sclerosis, fibrotic diseases, cancer, fever, psoriasis, cardiovascular diseases (*e.g.*, post-ischemic reperfusion injury and congestive heart failure), pulmonary diseases (*e.g.*, hyperoxic alveolar injury), hemorrhage, coagulation, radiation damage, and acute phase responses like those seen with infections and sepsis and during shock (*e.g.*, septic shock and hemodynamic shock). Chronic release of active TNF can cause cachexia and anorexia. And TNF can be lethal.

[5] TNF also has been implicated in infectious diseases. These include, for example, malaria, mycobacterial infection, meningitis. These also include viral infections, such as HIV, influenza virus, and herpes virus, including herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, human herpesvirus-6 (HHV-6), human herpesvirus-7 (HHV-7), human herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis, among others.

[6] IL-8 is another pro-inflammatory cytokine, which is produced by mononuclear cells, fibroblasts, endothelial cells, and keratinocytes. This cytokine is associated with conditions including inflammation.

[7] IL-1 is produced by activated monocytes and macrophages, and is involved in inflammatory responses. IL-1 plays a role in many pathophysiological responses, including rheumatoid arthritis, fever, and reduction of bone resorption.

[8] TNF, IL-1, and IL-8 affect a wide variety of cells and tissues, and are important inflammatory mediators of a wide variety of conditions. The inhibition of these cytokines by inhibition of the p38 kinase is beneficial in controlling, reducing, and alleviating many of these disease states.

[9] Various pyrazoles have previously been described:

[10] In U.S. Patent No. 4,000,281, Beiler and Binon report 4,5-aryl/heteroaryl substituted pyrazoles with antiviral activity against both RNA and DNA viruses, such as myxoviruses, adenoviruses, rhinoviruses, and various viruses of the herpes group.

[11] WIPO Int'l Publ. No. WO 92/19615 (published November 12, 1992) describes pyrazoles as novel fungicides.

[12] In U. S. Patent No. 3,984,431, Cueremy and Renault report derivatives of pyrazole-5-acetic acid as having anti-inflammatory activity, with [1-isobutyl-3,4-diphenyl-1H-pyrazol-5-yl]acetic acid being specifically described.

[13] In U. S. Patent No. 3,245,093, Hinsgen et al report a process for preparing pyrazoles.

[14] WIPO Int'l Publ. No. WO 83/00330 (published February 3, 1983) describes a process for preparing diphenyl-3,4-methyl-5-pyrazole derivatives.

[15] WIPO Int'l Publ. No. WO 95/06036 (published March 2, 1995 reports a process for preparing pyrazole derivatives.

[16] In U.S. patent 5,589,439, T. Goto, et al. report tetrazole derivatives and their use as herbicides.

[17] EP 515,041 reports pyrimidinyl substituted pyrazole derivatives as novel agricultural fungicides.

[18] Japanese Patent 4,145,081 reports pyrazolecarboxylic acid derivatives as herbicides.

[19] Japanese Patent 5,345,772 reports novel pyrazole derivatives as inhibiting acetylcholinesterase.

[20] Pyrazoles have been reported as useful in treating inflammation.

[21] Japanese Patent 5,017,470 reports synthesis of pyrazole derivatives as anti-inflammatory, anti-rheumatic, anti-bacterial, and anti-viral drugs.

[22] EP 115640 (published Dec 30, 1983) reports 4-imidazolyl-pyrazole derivatives as inhibitors of thromboxane synthesis, with 3-(4-Isopropyl-1-methylcyclohex-1-yl)-4-(imidazol-1-yl)-1H-pyrazole being specifically described.

[23] WIPO Int'l Publ. No. WO 97/01551 (published Jan 16, 1997) reports pyrazole compounds as adenosine antagonists, with 4-(3-Oxo-2,3-dihydropyridazin-6-yl)-3-phenylpyrazole being specifically described.

[24] In U.S. Patent No. 5,134,142, Matsuo et al. report 1,5-diaryl pyrazoles as having anti-inflammatory activity.

[25] In U.S. Patent No. 5,559,137, Adams et al. report pyrazoles (1,3,4,-substituted) as inhibitors of cytokines used in the treatment of cytokine diseases, with 3-(4-fluorophenyl)-1-(4-methylsulfinylphenyl)-4-(4-pyridyl)-5H-pyrazole being specifically described.

[26] WIPO Int'l Publ. No. WO 96/03385 (published February 8, 1996) reports 3,4-substituted pyrazoles as having anti-inflammatory activity, with 3-methylsulfonylphenyl-4-aryl-pyrazoles and 3-aminosulfonylphenyl-4-aryl-pyrazoles being specifically described.

[27] Laszlo et al., *Bioorg. Med. Chem. Letters*, 8 (1998) 2689-2694, describes certain furans, pyrroles, and pyrazolones (particularly 3-pyridyl-2,5-diaryl-pyrroles) as inhibitors of p38 kinase.

[28] WIPO Int'l Publ. No. WO 98/52940 (PCT Patent Application No. US98/10436 published on November 26, 1998) reports pyrazoles, compositions containing those pyrazoles, and methods for treating p38-mediated disorders using those pyrazoles.

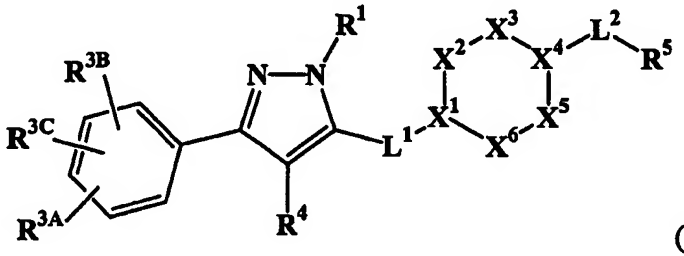
[29] WIPO Int'l Publ. No. WO 00/31063 (PCT Patent Application No. US99/26007 published on June 2, 2000) also reports pyrazoles, compositions containing those pyrazoles, and methods for treating p38-mediated disorders using those pyrazoles.

[30] In view of the importance of pyrazoles in the treatment of several pathological conditions (particularly those associated with p38 kinase activity, TNF activity, and/or cyclooxygenase-2 activity), there continues to be a need for pyrazole compounds exhibiting an improved safety profile, solubility, and/or potency. The following disclosure describes pyrazole compounds that tend to exhibit one or more such desirable qualities.

SUMMARY OF THE INVENTION

[31] This invention is directed to pyrazole compounds that tend to inhibit p38 kinase activity, TNF activity, and/or cyclooxygenase-2 activity. This invention also is directed to, for example, a method for inhibiting p38 kinase, TNF, and/or cyclooxygenase-2 activity, and particularly to a method for treating a condition (typically a pathological condition) mediated by p38 kinase activity, TNF activity, and/or cyclooxygenase-2 activity. Such a method is typically suitable for use with mammals, such as humans, other primates (*e.g.*, monkeys, chimpanzees. etc.), companion animals (*e.g.*, dogs, cats, horses. etc.), farm animals (*e.g.*, goats, sheep, pigs, cattle, etc.), laboratory animals (*e.g.*, mice, rats, etc.), and wild and zoo animals (*e.g.*, wolves, bears, deer, etc.).

[32] Briefly, therefore, this invention is directed, in part, to compounds that generally fall within structure of Formula I:



(I).

This invention also is directed to tautomers of such compounds, as well as salts (particularly pharmaceutically-acceptable salts) of such compounds and tautomers.

[33] In Formula (I):

[34] L^1 is a bond, -O-, -S-, -S(O)-, -$S(O)_2$-, -$N(R^a)$-, -C(O)-, -C(O)-$N(R^a)$-, -$N(R^a)$-C(O)-, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -C(H)=C(H)-, -C≡C-, -N=N-, -$N(R^a)$-$N(R^a)$-, -$N(R^a)$-C(O)-$N(R^a)$-, -C(S)-$N(R^a)$-, -$N(R^a)$-C(S)-, -CH_2-, -O-CH_2-, -CH_2-O-, -S-CH_2-, or -CH_2-S-.

[35] X^1 is nitrogen or carbon bonded to hydrogen, except that X^1 is carbon bonded to hydrogen if any of X^2, X^3, X^5, or X^6 is -NH- or -O-.

[36] X^2 is -CH_2-, -NH-, or -O-, except that X^2 is -CH_2- if X^3 is -O- or -NH-.

[37] X^3 is -CH_2-, -NH-, or -O-, except that X^3 is -CH_2- if X^2 is -O- or -NH-.

[38] X^4 is nitrogen or carbon bonded to hydrogen.

[39] X^5 is -CH_2- or -NH-, except that X^5 is -CH_2- if X^3 is -O- or X^6 is -NH-.

[40] X^6 is $-CH_2-$ or -NH-, except that X^6 is $-CH_2-$ if X^2 is -O- or X^5 is -NH-.

[41] R^1 is hydrogen, hydroxyalkyl, carboxyalkyl, aminoalkyl, aminocarbonylalkyl, or aminocarbonylaminoalkyl. The amino nitrogen(s) of the aminoalkyl, aminocarbonylalkyl, or aminocarbonylaminoalkyl optionally is/are substituted with up to two independently selected alkyl.

[42] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[43] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[44] R^{3C} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[45] R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino,

aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[46] L^2 is a bond, -O-, -S-, -S(O)-, -$S(O)_2$-, -$N(R^a)$-, -C(O)-, -C(O)-$N(R^a)$-, -$N(R^a)$-C(O)-, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -C(H)=C(H)-, -C≡C-, -N=N-, -$N(R^a)$-$N(R^a)$-, -$N(R^a)$-C(O)-$N(R^a)$-, -C(S)-$N(R^a)$-, -$N(R^a)$-C(S)-, -CH_2-, -O-CH_2-, -CH_2-O-, -S-CH_2-, or -CH_2-S-.

[47] Each R^a is independently selected from the group consisting of hydrogen and alkyl.

[48] R^5 is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonyloxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[49] This invention also is directed, in part, to a method for treating a condition mediated by pathological p38 kinase activity (particularly p38α activity) in a mammal. The method comprises administering an above-described compound, tautomer, or salt to the mammal in an amount that is therapeutically-effective to treat the condition.

[50] This invention also is directed, in part, to a method for treating a condition mediated by pathological TNF activity (particularly TNF-α activity) in a mammal. The method comprises administering an above-described compound, tautomer, or salt to the mammal in an amount that is therapeutically-effective to treat the condition.

[51] This invention also is directed, in part, to a method for treating a condition mediated by pathological cyclooxygenase-2 activity in a mammal. The method comprises administering an above-described compound, tautomer, or salt to the mammal in an amount that is therapeutically-effective to treat the condition.

[52] This invention also is directed, in part, to pharmaceutical compositions comprising a therapeutically-effective amount of an above-described compound, tautomer, or salt.

[53] This invention also is directed, in part, to a use of an above-described compound, tautomer, or salt to prepare a medicament for treating a condition mediated by p38 kinase activity.

[54] This invention also is directed, in part, to a use of an above-described compound, tautomer, or salt to prepare a medicament for treating a condition mediated by TNF activity.

[55] This invention also is directed, in part, to a use of an above-described compound, tautomer, or salt to prepare a medicament for treating a condition mediated by cyclooxygenase-2 activity.

[56] Further benefits of Applicants' invention will be apparent to one skilled in the art from reading this specification.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

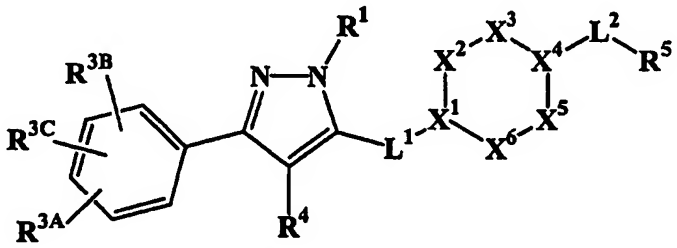
[57] This detailed description of preferred embodiments is intended only to acquaint others skilled in the art with Applicants' invention, its principles, and its practical application so that others skilled in the art may adapt and apply the invention in its numerous forms, as they may be best suited to the requirements of a particular use. This detailed description and its specific examples, while indicating preferred embodiments of this invention, are intended for purposes of illustration only. This invention, therefore, is

not limited to the preferred embodiments described in this specification, and may be variously modified.

A. Compounds of This Invention

[58] In accordance with this invention, it has been found that certain pyrazole compounds tend to be effective for inhibiting the activity (particularly pathological activity) of p38 kinase, TNF, and/or cyclooxygenase-2. Such compounds tend to exhibit desirable safety profiles, solubilities, and/or potencies.

[59] As noted above, the compounds of this invention generally have a structure corresponding to Formula I:



(I).

L^1, L^2, X^1, X^2, X^3, X^4, X^5, X^6, R^1, R^{3A}, R^{3B}, R^{3C}, R^4, and R^5 are defined as follows:

General Description of Preferred L^1 Substituents

[60] L^1 is a bond, -O-, -S-, -S(O)-, -$S(O)_2$-, -$N(R^a)$-, -C(O)-, -C(O)-$N(R^a)$-, -$N(R^a)$-C(O)-, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -C(H)=C(H)-, -C≡C-, -N=N-, -$N(R^a)$-$N(R^a)$-, -$N(R^a)$-C(O)-$N(R^a)$-, -C(S)-$N(R^a)$-, -$N(R^a)$-C(S)-, -CH_2-, -O-CH_2-, -CH_2-O-, -S-CH_2-, or -CH_2-S-.

[61] In some preferred embodiments, L^1 is a bond.

[62] Each R^a is independently selected from the group consisting of hydrogen and alkyl

[63] In some preferred embodiments, each R^a is alkyl.

[64] In some preferred embodiments, each R^a is hydrogen.

General Description of Preferred X^1, X^2, X^3, X^4, X^5, and X^6 Substituents

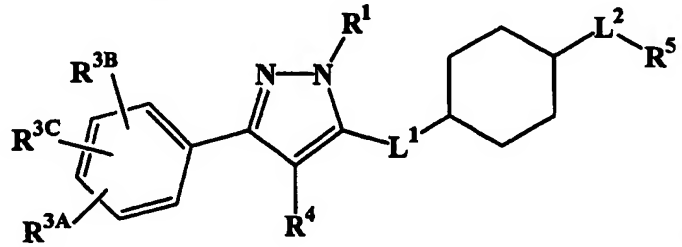
[65] X^1 is nitrogen or carbon bonded to hydrogen, except that X^1 is carbon bonded to hydrogen if any of X^2, X^3, X^5, or X^6 is -NH- or -O-. X^2 is -CH_2-, -NH-, or -O-,

except that X^2 is $-CH_2-$ if X^3 is -O- or -NH-. X^3 is $-CH_2-$, -NH-, or -O-, except that X^3 is $-CH_2-$ if X^2 is -O- or -NH-. X^4 is nitrogen or carbon bonded to hydrogen. X^5 is $-CH_2-$ or -NH-, except that X^5 is $-CH_2-$ if X^3 is -O- or X^6 is -NH-. And X^6 is $-CH_2-$ or -NH-, except that X^6 is $-CH_2-$ if X^2 is -O- or X^5 is -NH-.

[66] In some preferred embodiments, X^2, X^3, X^5, and X^6 are each $-CH_2-$.

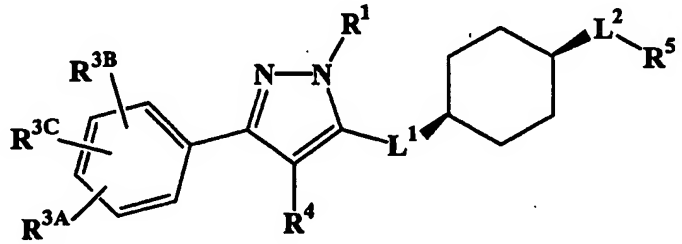
[67] In some preferred embodiments, X^1 and X^4 are each carbon bonded to hydrogen.

[68] In some preferred embodiments, the ring formed by X^1, X^2, X^3, X^4, X^5, and X^6 is cyclohexyl. In such embodiments, X^2, X^3, X^5, and X^6 are each $-CH_2-$; and X^1 and X^4 are each carbon bonded to hydrogen. In other words, the compound corresponds in structure to the following general formula:



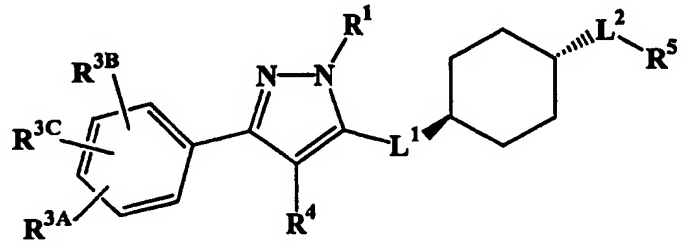
(I-A).

In some preferred embodiments, the compound has a cis configuration with respect to the cyclohexyl group:



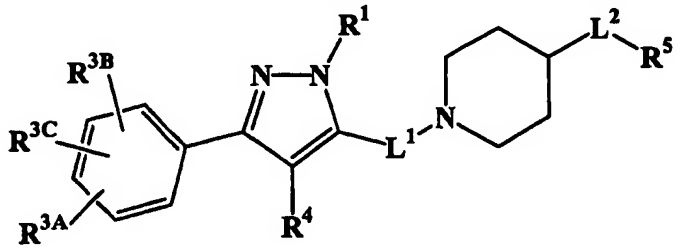
(I-B).

In typically more preferred embodiments, the compound has a trans configuration with respect to the cyclohexyl group:



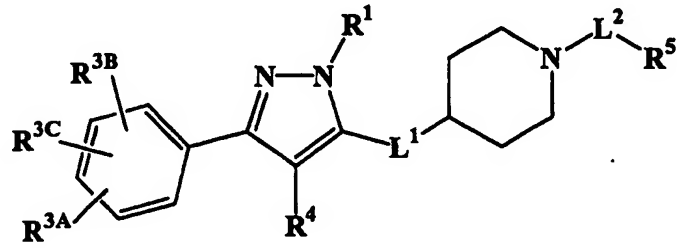
(I-C).

[69] In some preferred embodiments, the ring formed by X^1, X^2, X^3, X^4, X^5, and X^6 is piperidinyl. In some such embodiments, it is particularly preferred for X^2, X^3, X^5, and X^6 to each be $-CH_2-$; X^1 to be nitrogen; and X^4 to be carbon bonded to hydrogen. In other words, the compound corresponds in structure to the following general formula:



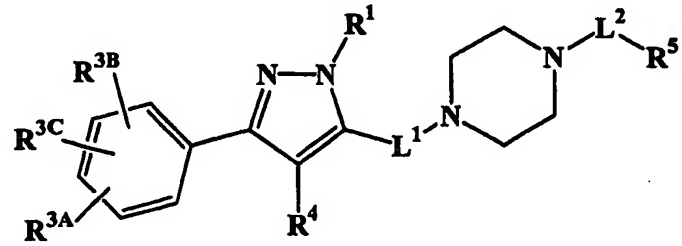
(I-D).

In other embodiments wherein the ring formed by X^1, X^2, X^3, X^4, X^5, and X^6 is piperidinyl, it is particularly preferred for X^2, X^3, X^5, and X^6 to each be $-CH_2-$; X^1 to be carbon bonded to hydrogen; and X^4 to be nitrogen. In other words, the compound corresponds in structure to the following general formula:



(I-E).

[70] In some preferred embodiments, the ring formed by X^1, X^2, X^3, X^4, X^5, and X^6 is piperazinyl. In some such embodiments, it is particularly preferred for X^2, X^3, X^5, and X^6 to each be $-CH_2-$; and X^1 and X^4 to each be nitrogen. In other words, the compound corresponds in structure to the following general formula:



(I-F).

General Description of Preferred R^1 Substituents

[71] R^1 is hydrogen, hydroxyalkyl, carboxyalkyl, aminoalkyl, aminocarbonylalkyl, or aminocarbonylaminoalkyl. The amino nitrogen(s) of the aminoalkyl, aminocarbonylalkyl, or aminocarbonylaminoalkyl optionally is/are substituted with up to two independently selected alkyl.

[72] In some preferred embodiments, R^1 is hydrogen.

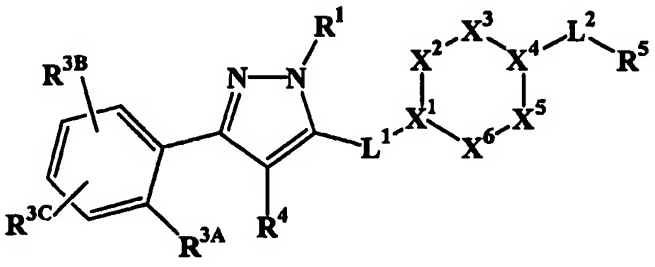
[73] In some preferred embodiments, R^1 is a non-hydrogen substituent that enhances solubility of the compound relative to the solubility of the compound if R^1 is hydrogen. One such particularly preferred R^1 substituent for enhancing solubility is hydroxyalkyl.

General Description of Preferred R^{3A} and R^{3B} Substituents

[74] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

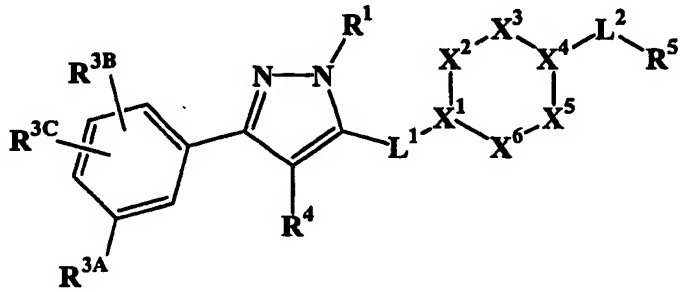
[75] In some preferred embodiments, R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[76] In some preferred embodiments, R^{3A} is at the ortho position of the 3-position phenyl ring in Formula I, *i.e.*, the compound corresponds in structure to the following formula:



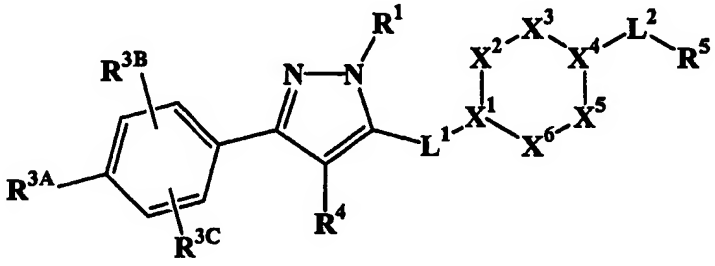
(I-G).

[77] In some preferred embodiments, R^{3A} is at the meta position of the 3-position phenyl ring in Formula I, *i.e.*, the compound corresponds in structure to the following formula:



(I-H).

[78] In some preferred embodiments, R^{3A} is at the para position of the 3-position phenyl ring in Formula I, *i.e.*, the compound corresponds in structure to the following formula:



(I-I).

[79] In some preferred embodiments, R^{3A} is hydroxy, cyano, amino, monomethylamino, monoethylamino, dimethylamino, diethylamino, N-methyl-N-ethyl-amino, methyl, ethyl, haloethyl, propyl, halopropyl, aminomethyl, aminoethyl, hydroxymethyl, hydroxyethyl, methoxy, halomethoxy, ethoxy, haloethoxy, methoxymethyl, or halomethoxymethyl.

[80] In some preferred embodiments, R^{3A} is hydroxy, cyano, amino, monomethylamino, monoethylamino, dimethylamino, diethylamino, N-methyl-N-ethyl-amino, methyl, ethyl, haloethyl, propyl, halopropyl, aminomethyl, aminoethyl, hydroxymethyl, hydroxyethyl, methoxy, ethoxy, haloethoxy, methoxymethyl, or halomethoxymethyl.

[81] In some preferred embodiments, R^{3A} is halogen, methyl, methoxy, halomethyl, or halomethoxy.

[82] In some preferred embodiments, R^{3A} is chloro, chloromethyl, or chloromethoxy.

[83] In some preferred embodiments, R^{3A} is fluoro, fluoromethyl, or fluoromethoxy.

[84] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[85] In some preferred embodiments, R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[86] In some preferred embodiments, R^{3B} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[87] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, chloro, methyl, trifluoromethyl, ethyl, hydroxy, methoxy, trifluoromethoxy, amino, monomethylamino, and dimethylamino.

[88] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of halogen, methyl, methoxy, halomethyl, and halomethoxy.

[89] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, fluoro, methyl, methoxy, chloromethyl, fluoromethyl, chloromethoxy, and fluoromethoxy.

[90] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, methyl, methoxy, chloromethyl, and chloromethoxy.

[91] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, methyl, methoxy, fluoromethyl, and fluoromethoxy.

[92] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, chloromethyl, and chloromethoxy.

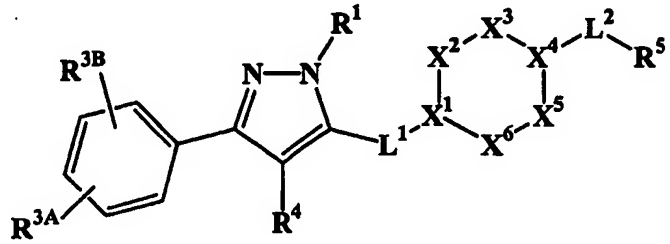
[93] In some preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, fluoromethyl, and fluoromethoxy.

[94] In some embodiments, R^{3A} is halogen or haloalkyl; and R^{3B} is hydrogen, halogen, or haloalkyl.

General Description of Preferred R^{3C} Substituents

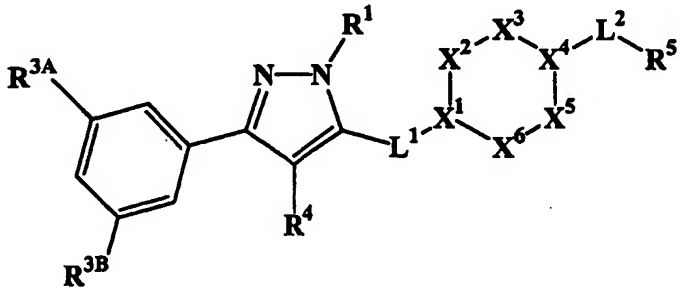
[95] R^{3C} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[96] In some preferred embodiments, R^{3C} is hydrogen. In other words, the compound corresponds in structure to the following formula:



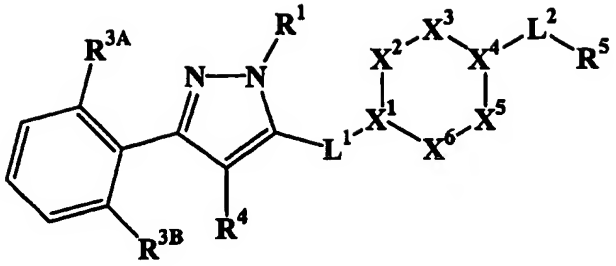
(I-J).

In some such embodiments, for example, the compound corresponds in structure to the following formula:



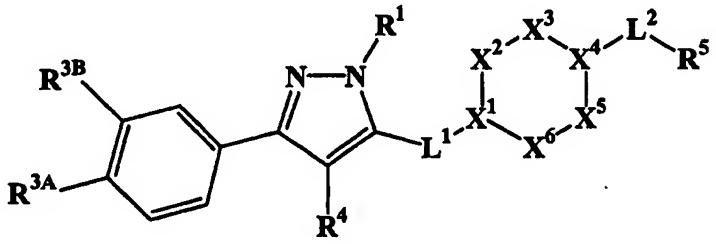
(I-K).

In other such embodiments, for example, the compound corresponds in structure to the following formula:



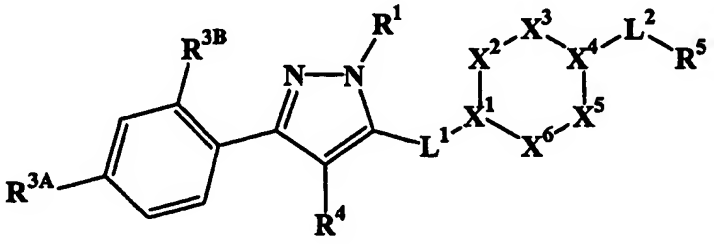
(I-L).

In other such embodiments, for example, the compound corresponds in structure to the following formula:



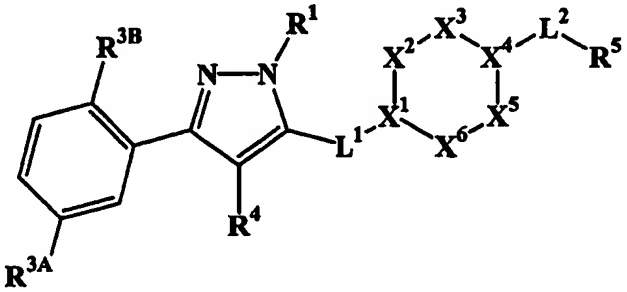
(I-M).

In other such embodiments, for example, the compound corresponds in structure to the following formula:



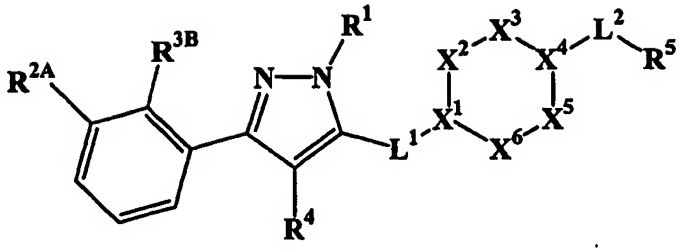
(I-N).

In other such embodiments, for example, the compound corresponds in structure to the following formula:



(I-O).

In other such embodiments, for example, the compound corresponds in structure to the following formula:



(I-P).

General Description of Preferred R^4 Substituents

[97] R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano,

alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[98] In some such preferred embodiments, R^4 is pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted as discussed above.

[99] In some such preferred embodiments, R^4 is pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted as discussed above.

[100] In some such preferred embodiments, R^4 is pyridazinyl, pyrazinyl, pyrimidinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, maleimidyl, pyridonyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted as discussed above.

[101] In some such preferred embodiments, R^4 is pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted as discussed above.

[102] In some such preferred embodiments, R^4 is a 6-member, nitrogen-containing ring that is optionally substituted as discussed above.

[103] In some such preferred embodiments, R^4 is pyrimidinyl or pyridinyl. The pyrimidinyl or pyridinyl optionally is substituted as discussed above.

[104] In some such preferred embodiments, R^4 is pyridinyl optionally substituted as discussed above.

[105] In some such preferred embodiments, R^4 is pyrimidinyl optionally substituted as discussed above.

[106] In some such preferred embodiments, R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted with alkylthio, mono-alkylamino, di-alkylamino, alkoxy, or haloalkoxy.

[107] In some such preferred embodiments, R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl.

[108] In some preferred embodiments, R^4 is pyrimidinyl optionally substituted with halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, or carbocyclylhydrazinyl. Any such optional substituent is, in turn,

optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[109] In some preferred embodiments, R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. These ring structures are:

substituted with one or more substituents independently selected from the group consisting of heterocyclyloxy, heterocyclylalkoxy, cycloalkylamino, cyanoaryloxy, alkylaminoalkylamino, and carbocyclylalkylheterocyclylamino, wherein:

any such substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy; and

optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, carbocyclylalkylamino, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylaminoalkylamino,

alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, heterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl, wherein:

any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[110] In some preferred embodiments, R^4 is pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. In these embodiments, any such substituent is:

substituted with one or more substituents independently selected from the group consisting of heterocyclyloxy, heterocyclylalkoxy, cycloalkylamino, cyanoaryloxy, alkylaminoalkylamino, and carbocyclylalkylheterocyclylamino, wherein:

any such substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy; and

optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, aminocarbonyl, alkoxy,

alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, carbocyclylalkylamino, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, heterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl, wherein:

any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[111] In some preferred embodiments, R^4 is pyrimidinyl. In these embodiments, the pyrimidinyl is:

substituted with one or more substituents independently selected from the group consisting of heterocyclyloxy, heterocyclylalkoxy, cycloalkylamino, cyanoaryloxy, alkylaminoalkylamino, and carbocyclylalkylheterocyclylamino, wherein:

any such substituent optionally is, in turn, substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy; and

optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy,

carbocyclylheterocyclyl, heterocyclylalkyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, carbocyclylalkylamino, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, heterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl, wherein:

any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[112] In some preferred embodiments, R^4 is pyrimidinyl substituted with heterocyclyloxy, heterocyclylalkoxy, cycloalkylamino, cyanoaryloxy, alkylaminoalkylamino, or carbocyclylalkylheterocyclylamino. Any such substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[113] In some preferred embodiments, R^4 is pyrimidinyl substituted with heterocyclyloxy, heterocyclylalkoxy, cycloalkylamino, cyanoaryloxy, dialkylaminoalkylamino, or carbocyclylalkylheterocyclylamino.

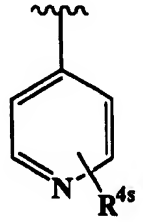
[114] In some preferred embodiments, R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent is substituted

with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[115] In some preferred embodiments, R^4 is pyridinyl substituted with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

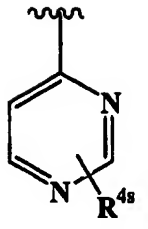
[116] In some preferred embodiments, R^4 is pyrimidinyl substituted with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[117] In some preferred embodiments, R^4 corresponds in structure to the following formula:

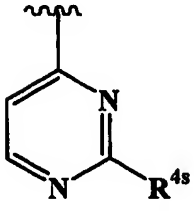


(I-Q).

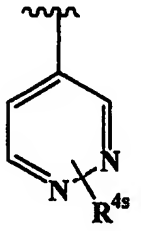
[118] In some preferred embodiments, R^4 corresponds in structure to the following formula:


(I-R).

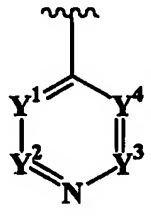
[119] In some preferred embodiments, R^4 corresponds in structure to the following formula:


(I-S).

[120] In some preferred embodiments, R^4 corresponds in structure to the following formula:

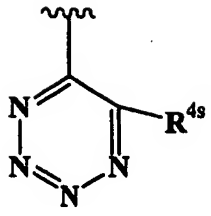

(I-T).

[121] In some preferred embodiments, R^4 corresponds in structure to the following formula:


(I-U).

Here, two of Y^1, Y^2, Y^3, and Y^4 are each nitrogen, one of Y^1, Y^2, Y^3, and Y^4 is carbon bonded to R^{4s}, and one of Y^1, Y^2, Y^3, and Y^4 is carbon bonded to hydrogen.

[122] In some preferred embodiments, R^4 corresponds in structure to the following formula:



(I-V).

[123] In the above embodiments, R^{4s} may be hydrogen, halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, or carbocyclylhydrazinyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[124] In some preferred embodiments, R^{4s} is hydrogen, alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, hetercycloalkylalkyl, heteroarylalkyl, amino, alkylamino, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, heterocycloalkylamino, heteroarylamino, hydroxy, alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, heterocycloalkyloxy, or heteroaryloxy. Any such substituent optionally is substituted with

one or more substituents independently selected from the group consisting of hydroxy and alkyl.

[125] In some preferred embodiments, R^{4s} is hydrogen, C_1-C_4-alkyl, aminopropyl, monomethylaminopropyl, dimethylaminopropyl, hydroxypropyl, methoxypropyl, cyclopentylmethyl, pyrrolidinylmethyl, tetrahydrofuranylmethyl, piperidinylmethyl, tetrahydropyranylmethyl, pyridinylmethyl, C_1-C_3-alkylamino, aminoethylamino, monomethylaminoethylamino, dimethylaminoethylamino, hydroxyethylamino, methoxyethylamino, cyclopentylamino, pyrrolidinylamino, tetrahydrofuranylamino, piperidinylamino, tetrahydropyranylamino, pyridinylamino, C_1-C_3-alkoxy, aminoethoxy, monomethylaminoethoxy, dimethylaminoethoxy, hydroxyethoxy, methoxyethoxy, cyclopentyloxy, pyrrolidinyloxy, tetrahydrofuranyloxy, piperidinyloxy, tetrahydropyranyloxy, or pyridinyloxy. Any pyrrolidinyl nitrogen or piperidinyl nitrogen optionally is substituted with methyl.

[126] In some preferred embodiments, R^{4s} is C_1-C_4-alkyl, aminopropyl, monomethylaminopropyl, dimethylaminopropyl, hydroxypropyl, methoxypropyl, cyclopentylmethyl, pyrrolidinylmethyl, tetrahydrofuranylmethyl, piperidinylmethyl, tetrahydropyranylmethyl, pyridinylmethyl, C_1-C_3-alkylamino, aminoethylamino, monomethylaminoethylamino, dimethylaminoethylamino, hydroxyethylamino, methoxyethylamino, cyclopentylamino, pyrrolidinylamino, tetrahydrofuranylamino, piperidinylamino, tetrahydropyranylamino, pyridinylamino, C_1-C_3-alkoxy, aminoethoxy, monomethylaminoethoxy, dimethylaminoethoxy, hydroxyethoxy, methoxyethoxy, cyclopentyloxy, pyrrolidinyloxy, tetrahydrofuranyloxy, piperidinyloxy, tetrahydropyranyloxy, or pyridinyloxy. Any pyrrolidinyl nitrogen or piperidinyl nitrogen optionally is substituted with methyl.

[127] In some preferred embodiments, R^{4s} is hydrogen, alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, arylalkyl, hetercycloalkylalkyl, heteroarylalkyl, amino, alkylamino, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, arylamino, heterocycloalkylamino, heteroarylamino, hydroxy, alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, aryloxy, heterocycloalkyloxy, heteroaryloxy, thiol, alkylthio, cycloalkylthio, arylthio, heterocycloalkylthio, heteroarylthio, aminosulfonyl, alkylsulfonyl, cycloalkylsulfonyl, arylsulfonyl, heterocycloalkylsulfonyl, or

heteroarylsulfonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy, cyano, and alkyl.

[128] In some preferred embodiments, R^{4s} is hydrogen, C_1-C_6-alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, hetercycloalkylalkyl, heteroarylalkyl, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, heterocycloalkylamino, heteroarylamino, hydroxy, C_2-C_6-alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, heterocycloalkyloxy, heteroaryloxy, thiol, C_2-C_6-alkylthio, cycloalkylthio, heterocycloalkylthio, heteroarylthio, aminosulfonyl, C_2-C_6-alkylsulfonyl, cycloalkylsulfonyl, heterocycloalkylsulfonyl, or heteroarylsulfonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy, cyano, and alkyl.

[129] In some preferred embodiments, R^{4s} is C_1-C_6-alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, hetercycloalkylalkyl, heteroarylalkyl, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, heterocycloalkylamino, heteroarylamino, hydroxy, C_2-C_6-alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, heterocycloalkyloxy, heteroaryloxy, thiol, C_2-C_6-alkylthio, cycloalkylthio, heterocycloalkylthio, heteroarylthio, aminosulfonyl, C_2-C_6-alkylsulfonyl, cycloalkylsulfonyl, heterocycloalkylsulfonyl, or heteroarylsulfonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy, cyano, and alkyl.

[130] In some preferred embodiments, R^{4s} is alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[131] In some preferred embodiments, R^{4s} is alkoxycarbonyl, carbocyclyloxycarbonyl, or heterocyclyloxycarbonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro,

cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[132] In some preferred embodiments, R^{4s} is alkylaminocarbonyl optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[133] In some preferred embodiments, R^{4s} is $-CH_2OH$, $-C(CH_3)(H)-OH$, or $-C(CH_3)_2-OH$.

[134] In some preferred embodiments, R^{4s} is aminomethyl. In these embodiments, the amino nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, haloalkyl, alkylsulfonyl, alkoxyalkyl, and heterocyclyl.

[135] In some preferred embodiments, R^{4s} is hydrogen, alkylthio, mono-alkylamino, di-alkylamino, alkoxy, or haloalkoxy.

[136] In some preferred embodiments, R^{4s} is alkylthio, mono-alkylamino, di-alkylamino, alkoxy, or haloalkoxy.

[137] In some preferred embodiments, R^{4s} is heterocyclyloxy, heterocyclylalkoxy, cycloalkylamino, cyanoaryloxy, dialkylaminoalkylamino, or carbocyclylalkylheterocyclylamino.

[138] In some preferred embodiments, R^{4s} is tetrahydrofuranyloxy, cyanophenyloxy, morpholinylethyloxy, cyclopentylamino, dimethylaminoethylamino, or phenylmethylpiperidinylamino.

[139] In some preferred embodiments, R^{4s} is alkylaminoalkoxy.

[140] In some preferred embodiments, R^{4s} is dialkylaminoalkoxy.

[141] In some preferred embodiments, R^{4s} is dimethylaminoethoxy.

[142] In some preferred embodiments, R^{4s} is hydrogen.

General Description of Preferred L^2 and R^5 Substituents

[143] L^2 is a bond, -O-, -S-, -S(O)-, $-S(O)_2-$, $-N(R^a)-$, -C(O)-, -C(O)-$N(R^a)$-, $-N(R^a)-C(O)-$, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -C(H)=C(H)-, -C≡C-, -N=N-,

$-N(R^a)-N(R^a)-$, $-N(R^a)-C(O)-N(R^a)-$, $-C(S)-N(R^a)-$, $-N(R^a)-C(S)-$, $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-S-CH_2-$, or $-CH_2-S-$.

[144] Each R^a is independently selected from the group consisting of hydrogen and alkyl.

[145] In some preferred embodiments, each R^a is hydrogen.

[146] In other preferred embodiments, each R^a is alkyl.

[147] In some preferred embodiments, L^2 is $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N(R^a)-$, $-C(O)-$, $-C(O)-N(R^a)-$, $-N(R^a)-C(O)-$, $-C(O)-O-$, $-O-C(O)-$, $-O-C(O)-O-$, $-C(H)=C(H)-$, $-C\equiv C-$, $-N=N-$, $-N(R^a)-N(R^a)-$, $-N(R^a)-C(O)-N(R^a)-$, $-C(S)-N(R^a)-$, $-N(R^a)-C(S)-$, $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-S-CH_2-$, or $-CH_2-S-$.

[148] In some preferred embodiments, L^2 is a bond, $-O-$, $-S-$, $-S(O)-$, $-N(R^a)-$, $-N(R^a)-C(O)-$, $-O-C(O)-$, $-O-C(O)-O-$, $-C(H)=C(H)-$, $-C\equiv C-$, $-N=N-$, $-N(R^a)-N(R^a)-$, $-N(R^a)-C(O)-N(R^a)-$, $-C(S)-N(R^a)-$, $-N(R^a)-C(S)-$, $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-S-CH_2-$, or $-CH_2-S-$.

[149] In some preferred embodiments, $-L^2$ is $-C(O)-$.

[150] In some preferred embodiments, $-L^2$ is $-O-$.

[151] In some preferred embodiments, L^2 is $-N(R^a)-$.

[152] In some preferred embodiments, L^2 is a bond.

[153] R^5 is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkylcarbonyloxyalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent is optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[154] In some preferred embodiments, R^5 is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent is optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[155] In some preferred embodiments, R^5 is hydrogen, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent optionally is

substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[156] In some preferred embodiments, R^5 is alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[157] In some preferred embodiments, R^5 is hydrogen, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl.

[158] In some preferred embodiments, R^5 is hydrogen, alkenyl, or alkylcarbonylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkoxy, and haloalkoxy.

[159] In some preferred embodiments, R^5 is alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonyloxyalkyl, or tetrahydrofuranylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy and halogen.

[160] In some preferred embodiments, R^5 is alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, or tetrahydrofuranylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy and halogen.

[161] In some preferred embodiments, R^5 is haloalkyl, hydroxyalkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[162] In some preferred embodiments, R^5 is phosphonooxyalkyl, monoalkylphosphonooxyalkyl, dialkylphosphonooxyalkyl, aminoalkylcarbonyloxyalkyl,

monoalkylaminoalkylcarbonyloxyalkyl, dialkylaminoalkylcarbonyloxyalkyl, phenylalkyl substituted with alkylcarbonyloxy, or tetrahydrofuranyl.

[163] In some preferred embodiments, R^5 is hydrogen, alkenyl, or alkylcarbonylalkyl.

[164] In some preferred embodiments, R^5 is hydroxyalkyl, *i.e.*, alkyl substituted with one or more hydroxy radicals (often only one hydroxy radical).

[165] In some preferred embodiments, R^5 is C_1-C_6-hydroxyalkyl.

[166] In some preferred embodiments, R^5 is hydroxymethyl.

[167] In some preferred embodiments, R^5 is alkylcarbonyloxyalkyl.

[168] In some preferred embodiments, R^5 is methylcarbonyloxymethyl.

[169] In some preferred embodiments, R^5 is hydrogen.

[170] In some preferred embodiments, R^5 is heterocyclyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[171] In some preferred embodiments, R^5 is carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

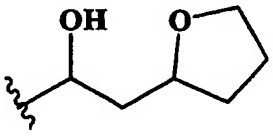
[172] In some preferred embodiments, R^5 is substituted methyl. The methyl is substituted with:

two substituents independently selected from the group consisting of hydroxy, alkoxy, hydroxymethyl, hydroxyethyl, alkoxymethyl, alkoxyethyl, tetrahydrofuranyl, and tetrahydrofuranylmethyl, wherein any such substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy; or

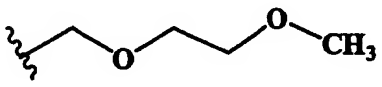
a substituent selected from the group consisting of alkoxyethoxy, hydroxyethoxy, alkoxypropoxy, and hydroxypropoxy, wherein any such substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

The methyl optionally is further substituted with hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[173] In some preferred embodiments, R^5 is a radical corresponding in structure to one of the following formulas:



(I-W-1),



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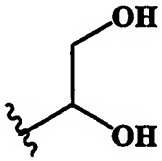
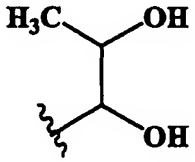
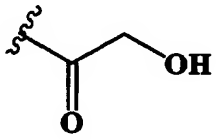


(I-W-3), and

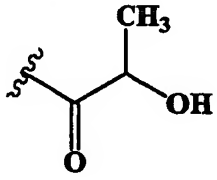


(I-W-4).

[174] In some preferred embodiments, $-L^2-R^5$ is a radical corresponding in structure to one of the following formulas:



(I-X-1),



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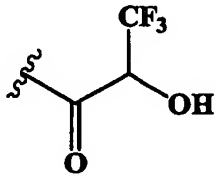

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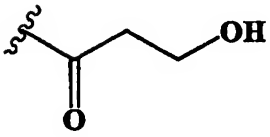
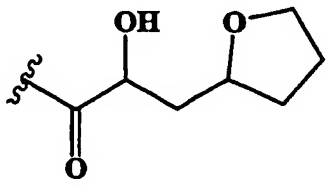
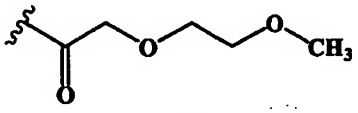


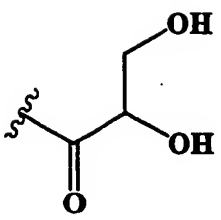
(I-X-4),



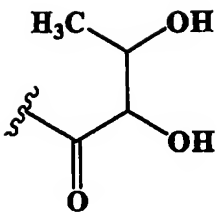
(I-X-5),



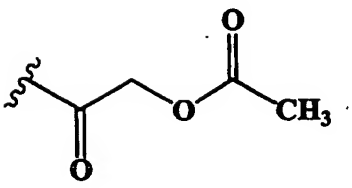
(I-X-6),



(I-X-8),

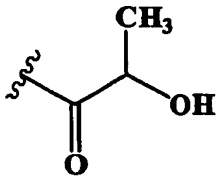


(I-X-9), and

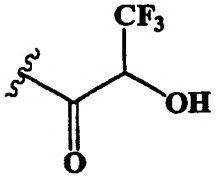


(I-X-10).

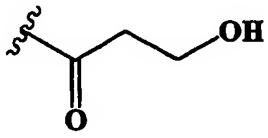
[175] In some preferred embodiments, $-L^2-R^5$ is a radical corresponding in structure to one of the following formulas:



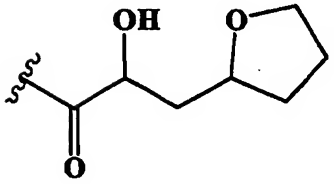
(I-Y-1),



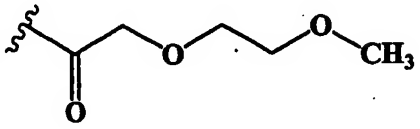
(I-Y-2),



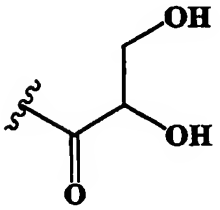
(I-Y-3),



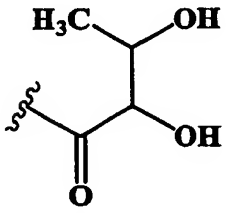
(I-Y-4),



(I-Y-5),



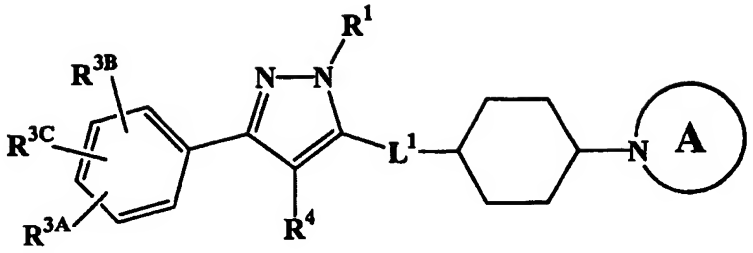
(I-Y-6), and



(I-Y-7).

[176] In some preferred embodiments, L^2 is a bond; and R^5 is heterocyclyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[177] In some preferred embodiments, the compound corresponds in structure to the following formula:



(I-Z).

Here, the ring structure A is a heterocyclyl ring that contains a nitrogen bonded to the cyclohexyl. The is heterocyclyl ring also is optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[178] In some preferred embodiments, L^2 is $-N(R^a)-$; and R^5 is alkyl, carbocyclyl, or carbocyclylalkyl. The alkyl, carbocyclyl, or carbocyclylalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[179] In some preferred embodiments, $-L^2-R^5$ is hydroxyalkylcarbonyl, *i.e.*, alkylcarbonyl substituted with one or more hydroxy radicals (often only one hydroxy radical).

[180] In some preferred embodiments, $-L^2-R^5$ is hydroxymethylcarbonyl.

[181] In some preferred embodiments, $-L^2-R^5$ is alkylcarbonyloxyalkylcarbonyl.

[182] In some preferred embodiments, $-L^2-R^5$ is methylcarbonyloxymethylcarbonyl.

[183] In some preferred embodiments, $-L^2-R^5$ is hydroxy.

[184] In some preferred embodiments, $-L^2-R^5$ is hydrogen, methyl, or butyloxycarbonyl.

[185] In some preferred embodiments, $-L^2-R^5$ is hydrogen or alkyl.

Detailed Description of Several Preferred Embodiments

[186] The above discussion describes the compounds of this invention in general terms. The following discussion, in turn, describes in detail several specific preferred and particularly preferred embodiments.

Preferred Embodiment No. 1

[187] In some preferred embodiments:

[188] L^2 is -O-, -S-, -S(O)-, -$S(O)_2$-, -$N(R^a)$-, -C(O)-, -C(O)-$N(R^a)$-, -$N(R^a)$-C(O)-, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -C(H)=C(H)-, -C≡C-, -N=N-, -$N(R^a)$-$N(R^a)$-, -$N(R^a)$-C(O)-$N(R^a)$-, -C(S)-$N(R^a)$-, -$N(R^a)$-C(S)-, -CH_2-, -O-CH_2-, -CH_2-O-, -S-CH_2-, or -CH_2-S-.

[189] R^{3A} and R^{3B} are independently selected from the group consisting of halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, and alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

Particularly Preferred Compounds of Embodiment No. 1

[190] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[191] In some particularly preferred embodiments, R^1 is hydrogen.

[192] In some particularly preferred embodiments, L^1 is a bond.

[193] In some particularly preferred embodiments, R^{3C} is hydrogen.

[194] In some particularly preferred embodiments, X^2, X^3, X^5, and X^6 are each -CH_2-.

[195] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, chloro, methyl, trifluoromethyl, ethyl, hydroxy, methoxy, trifluoromethoxy, amino, monomethylamino, and dimethylamino.

[196] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of halogen, methyl, methoxy, halomethyl, and halomethoxy.

[197] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, fluoro, methyl, methoxy, chloromethyl, fluoromethyl, chloromethoxy, and fluoromethoxy.

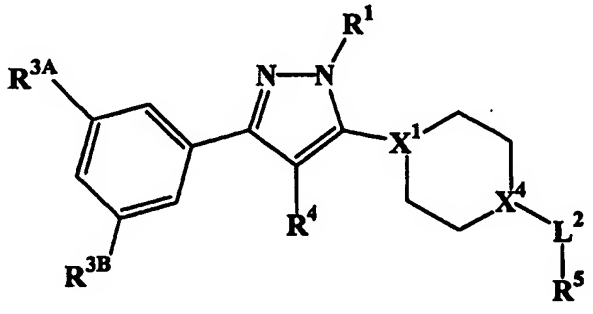
[198] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, methyl, methoxy, chloromethyl, and chloromethoxy.

[199] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, methyl, methoxy, fluoromethyl, and fluoromethoxy.

[200] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, chloromethyl, and chloromethoxy.

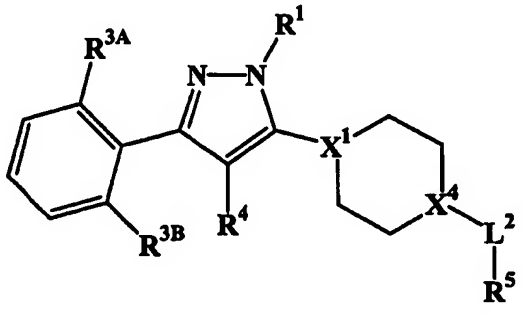
[201] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, fluoromethyl, and fluoromethoxy.

[202] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



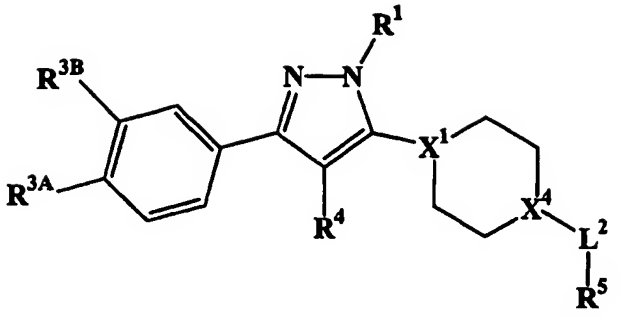
(18-1).

[203] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



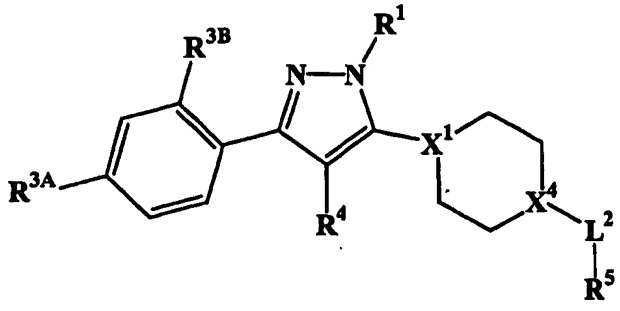
(19-1).

[204] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



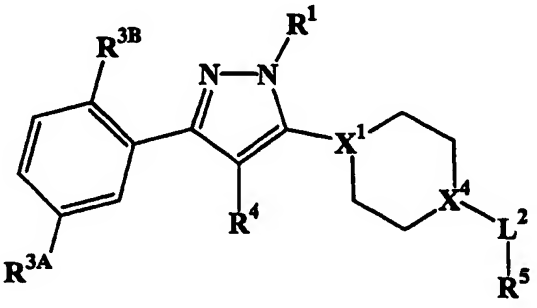
(20-1).

[205] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



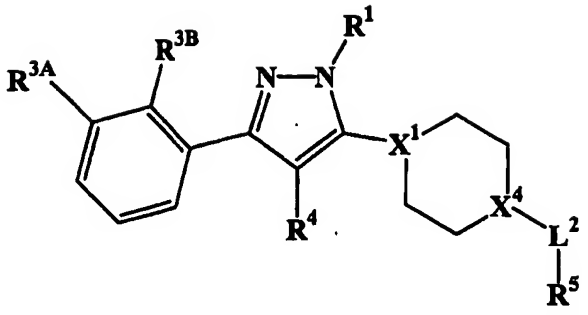
(21-1).

[206] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



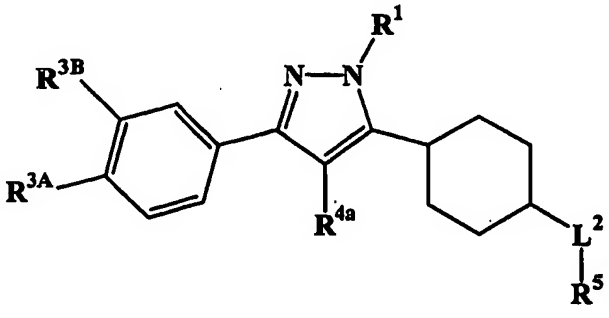
(23-1).

[207] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



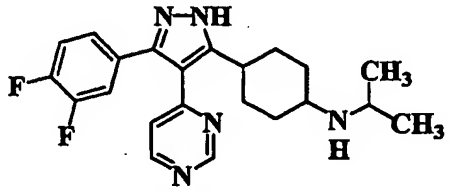
(24-1).

[208] In some particularly preferred embodiments, X^1 and X^4 are each carbon bonded to hydrogen. In some such embodiments, the compound corresponds in structure to the following formula:



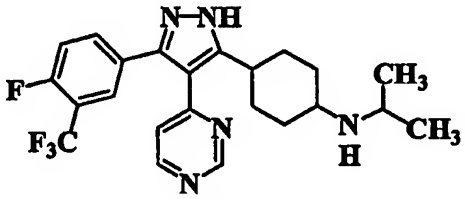
(26-1).

Examples of such compounds include those corresponding in structure to the following formulas:



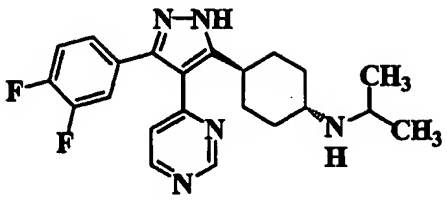
(27-1)

and



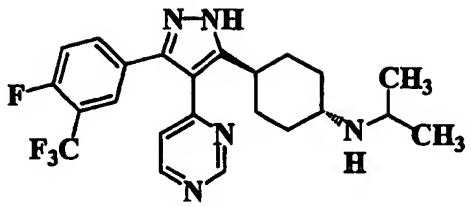
(27-2).

In some embodiments, the preferred geometrical isomers have the trans configuration with respect to the cyclohexyl group. Thus, for example, the preferred geometrical isomers of the compounds of Formulas (27-1) and (27-2) are the following, respectively:



(27-1A)

and

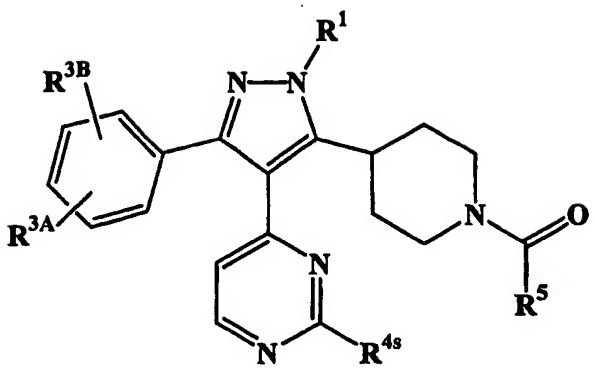


(27-2A).

[209] In some particularly preferred embodiments, $-L^2$ is -C(O)-.

[210] In some particularly preferred embodiments, R^4 is pyrimidinyl optionally substituted with halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, or carbocyclylhydrazinyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[211] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(30-1).

[212] In some such embodiments, R^{4s} is hydrogen, alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, hetercycloalkylalkyl, heteroarylalkyl, amino, alkylamino, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, heterocycloalkylamino, heteroarylamino, hydroxy, alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, heterocycloalkyloxy, or heteroaryloxy. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy and alkyl.

[213] In other such embodiments, R^{4s} is hydrogen, C_1-C_4-alkyl, aminopropyl, monomethylaminopropyl, dimethylaminopropyl, hydroxypropyl, methoxypropyl, cyclopentylmethyl, pyrrolidinylmethyl, tetrahydrofuranylmethyl, piperidinylmethyl, tetrahydropyranylmethyl, pyridinylmethyl, C_1-C_3-alkylamino, aminoethylamino, monomethylaminoethylamino, dimethylaminoethylamino, hydroxyethylamino, methoxyethylamino, cyclopentylamino, pyrrolidinylamino, tetrahydrofuranylamino, piperidinylamino, tetrahydropyranylamino, pyridinylamino, C_1-C_3-alkoxy, aminoethoxy, monomethylaminoethoxy, dimethylaminoethoxy, hydroxyethoxy, methoxyethoxy, cyclopentyloxy, pyrrolidinyloxy, tetrahydrofuranyloxy, piperidinyloxy, tetrahydropyranyloxy, or pyridinyloxy. Any pyrrolidinyl nitrogen or piperidinyl nitrogen optionally is substituted with methyl.

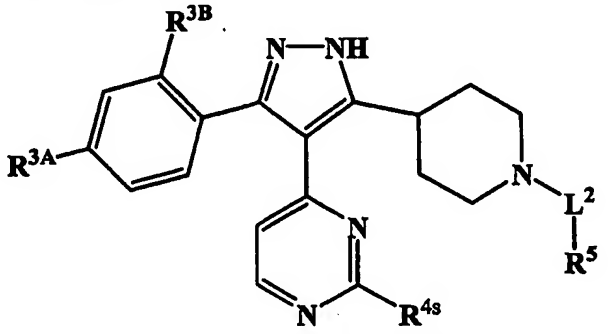
[214] In some particularly preferred embodiments, R^4 is pyridinyl, pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent is

substituted with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[215] In some particularly preferred embodiments, R^4 is pyridinyl substituted with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[216] In some particularly preferred embodiments, R^4 is pyrimidinyl substituted with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[217] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(8-1).

In these embodiments, R^{4s} is alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent optionally is

substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[218] In some such embodiments, R^{4s} is alkoxycarbonyl, carbocyclyloxycarbonyl, or heterocyclyloxycarbonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

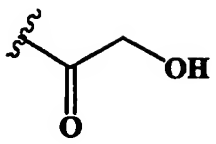
[219] In some other such embodiments, R^{4s} is alkylaminocarbonyl optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[220] In some other such embodiments, R^{4s} is $-CH_2OH$, $-C(CH_3)(H)-OH$, or $-C(CH_3)_2-OH$.

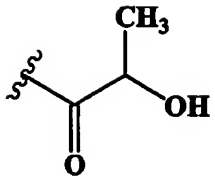
[221] In some other such embodiments, R^{4s} is aminomethyl. In these embodiments, the amino nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, haloalkyl, alkylsulfonyl, alkoxyalkyl, and heterocyclyl.

[222] In some particularly preferred embodiments, R^5 is alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonyloxyalkyl, or tetrahydrofuranylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy and halogen.

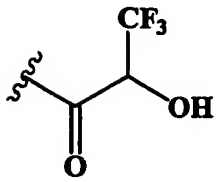
[223] In some particularly preferred embodiments, $-L^2-R^5$ is a radical corresponding in structure to one of the following formulas:



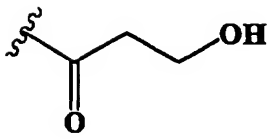
(33-1),



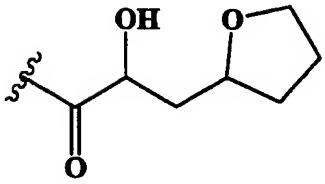
(33-2),



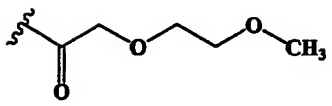
(33-3),



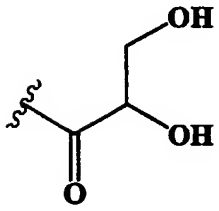
(33-4),



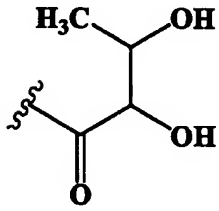
(33-5),



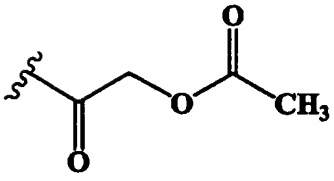
(33-6),



(33-8),



(33-9), and

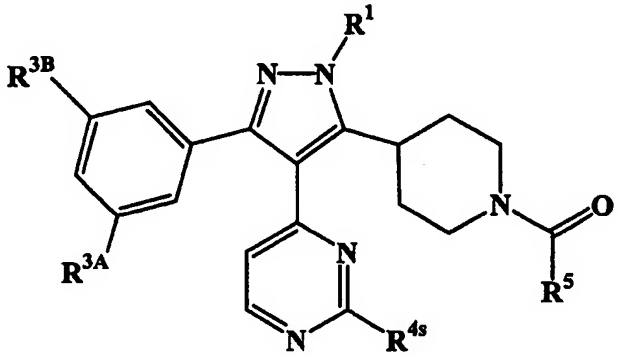


(33-10).

[224] In some particularly preferred embodiments, $-L^2-R^5$ is hydroxyalkylcarbonyl.

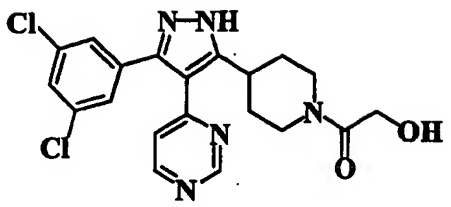
[225] In some particularly preferred embodiments, $-L^2-R^5$ is hydroxymethylcarbonyl.

[226] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

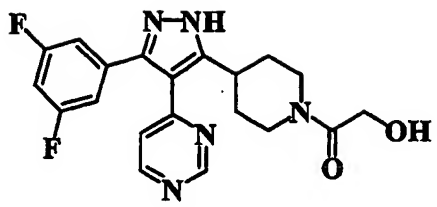


(35-1).

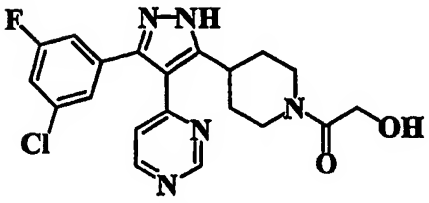
Examples of such compounds include those corresponding in structure to the following formulas:



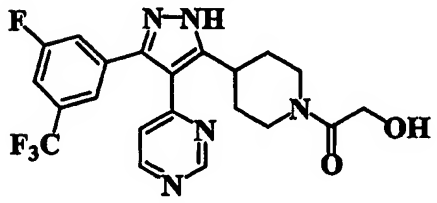
(36-1),



(36-2),

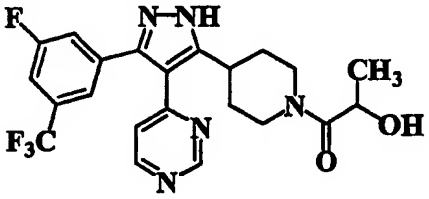


(36-3), and

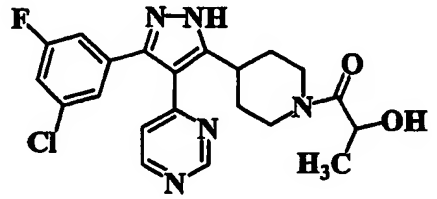


(36-4).

Additional examples of such compounds include those corresponding in structure to the following formulas:

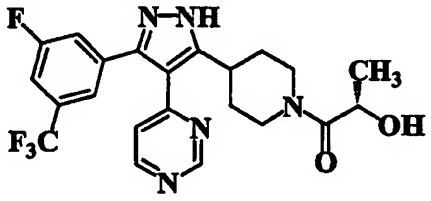


(36-5), and



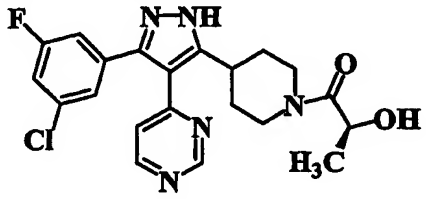
(36-6).

In some embodiments, the preferred optical isomer of the compound of Formula (36-5) corresponds in structure to the following formula:



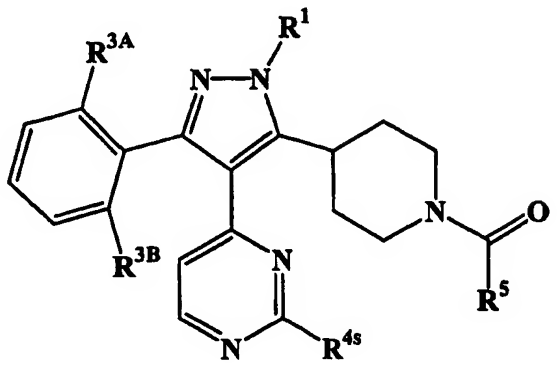
(36-5A).

In some embodiments, the preferred optical isomer of the compound of Formula (36-6) corresponds in structure to the following formula:



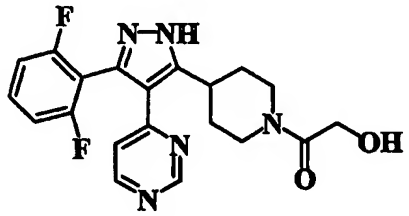
(36-6A).

[227] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



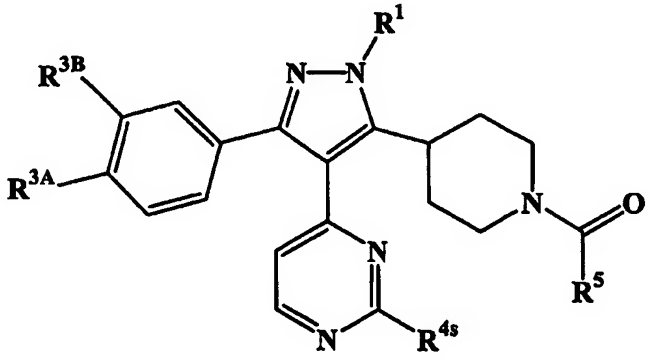
(37-1).

One such compound, for example, corresponds in structure to the following formula:



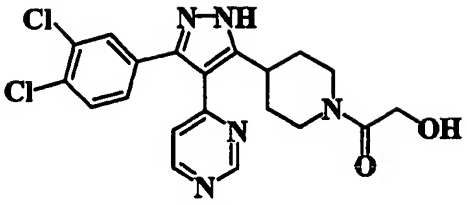
(38-1).

[228] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

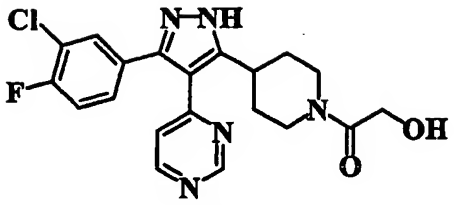


(39-1).

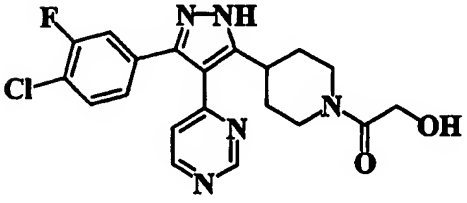
Examples of such compounds include those corresponding in structure to the following formulas:



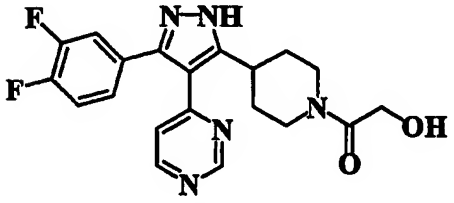
(40-1),



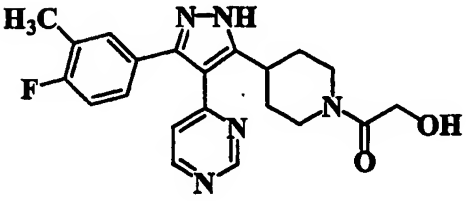
(40-2),



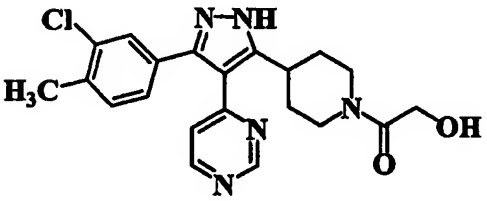
(40-3),



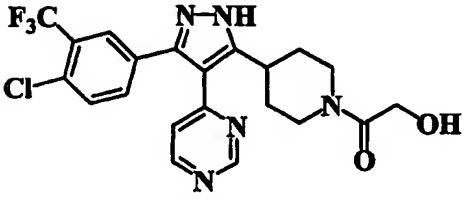
(40-4),



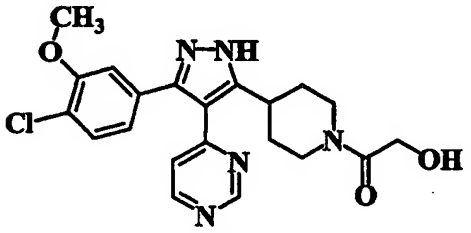
(40-5),



(40-6),

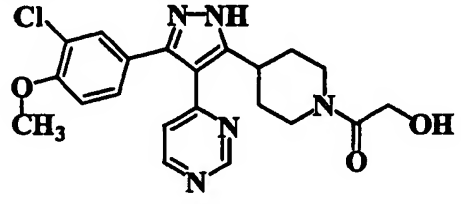


(40-7), and

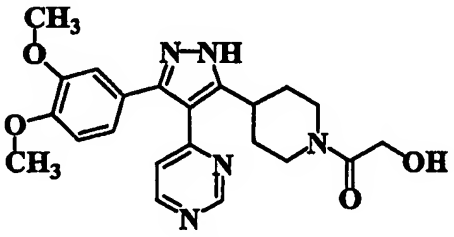


(40-8).

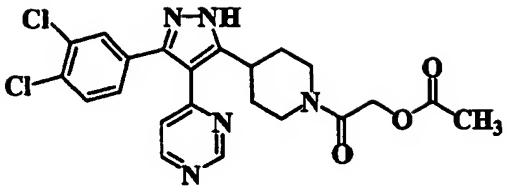
Additional examples of such compounds include those corresponding in structure to the following formulas:



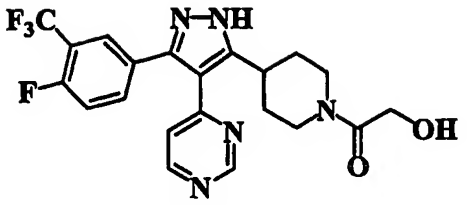
(40-9),



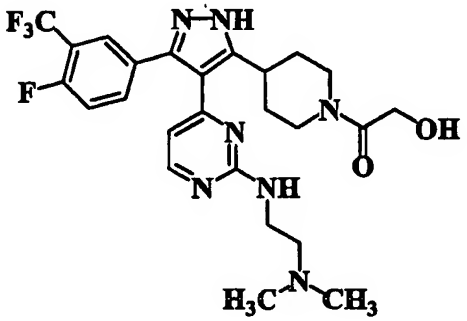
(40-10),



(40-11),

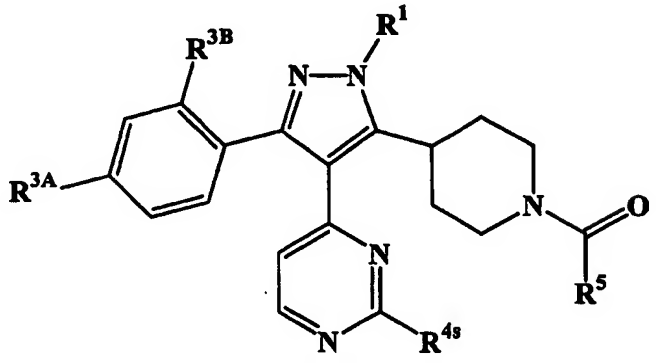


(40-12), and



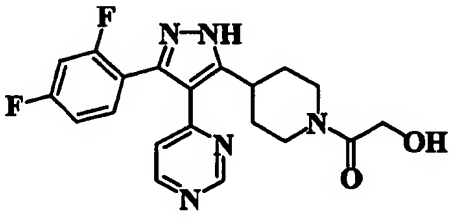
(40-13).

[229] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

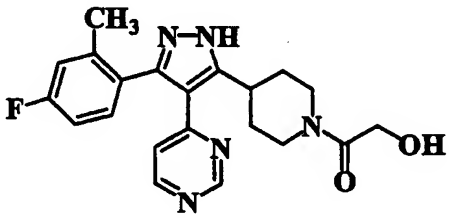


(42-1).

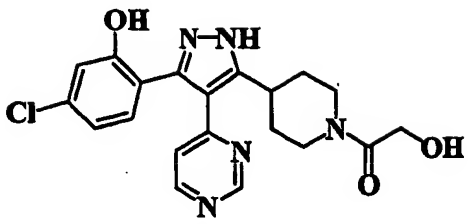
Examples of such compounds include those corresponding in structure to the following formulas:



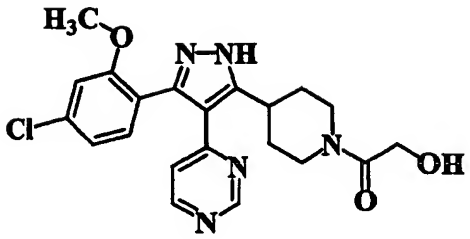
(43-1),



(43-2),

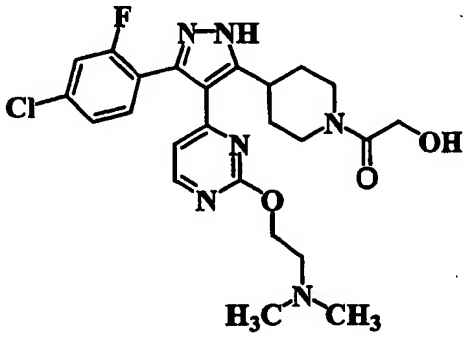


(43-3), and

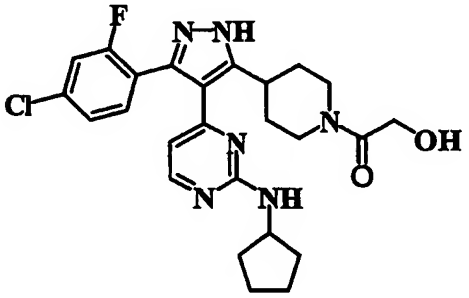


(43-4).

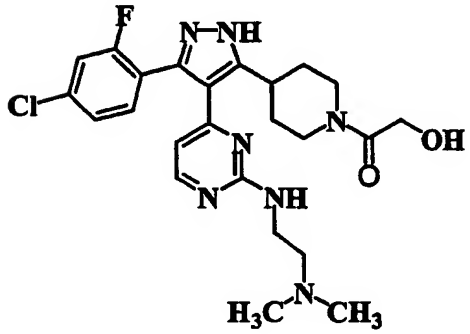
Examples of such compounds also include those corresponding in structure to the following formulas:



(43-5),

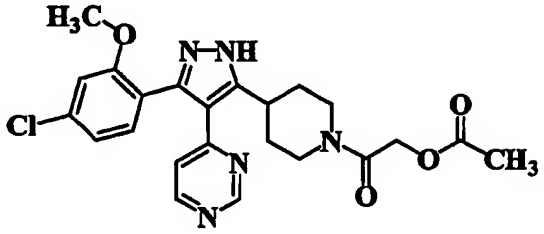


(43-6), and



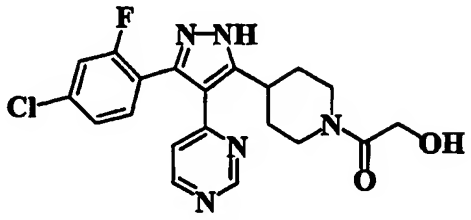
(43-7).

An additional example of such compounds includes the compound corresponding in structure to the following formula:



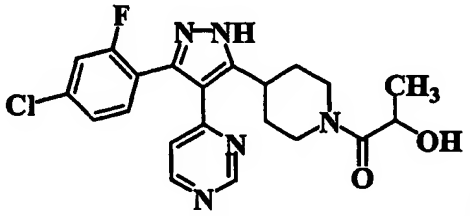
(44-1).

An additional example of such compounds includes the compound corresponding in structure to the following formula:



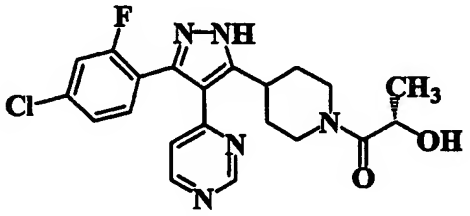
(45-1).

An additional example of such compounds includes the compound corresponding in structure to the following formula:



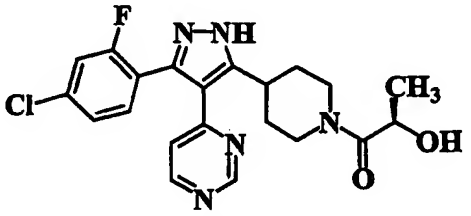
(46-1).

In some embodiments, this compound corresponds in structure to the following optical isomer:



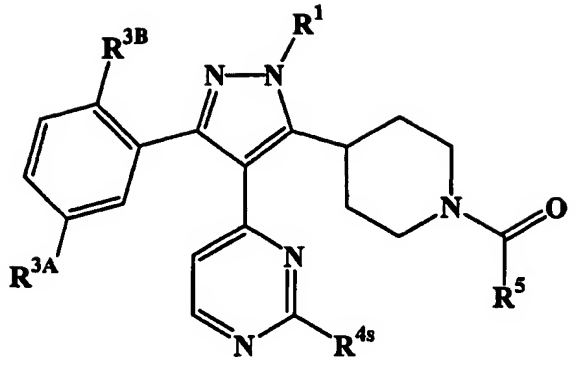
(46-1A).

In other embodiments, the compound corresponds in structure to the following optical isomer:



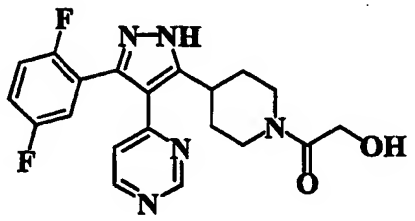
(46-1B)

[230] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

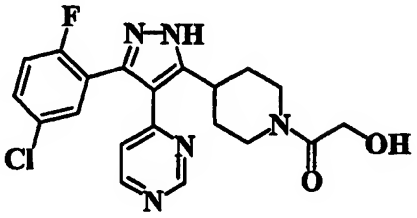


(47-1).

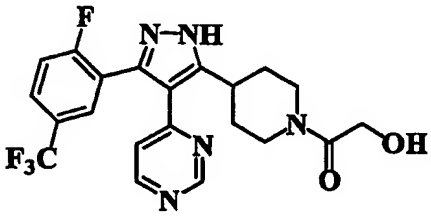
Examples of such compounds include those corresponding in structure to the following formulas:



(48-1),

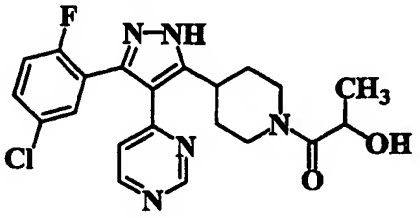


(48-2), and

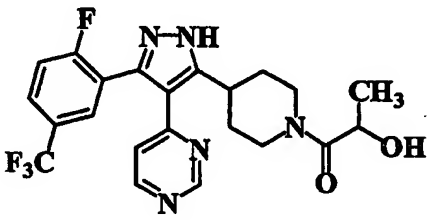


(48-3).

Additional examples of such compounds include those corresponding in structure to the following formulas:

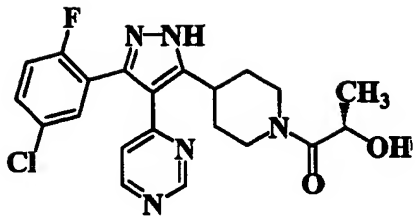


(48-4), and



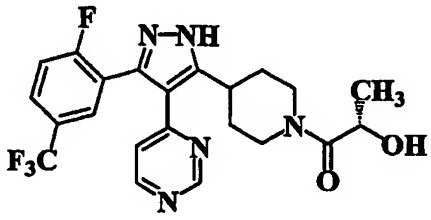
(48-5).

In some embodiments, the preferred optical isomer of the compound of Formulas (48-4) corresponds in structure to the following formula:



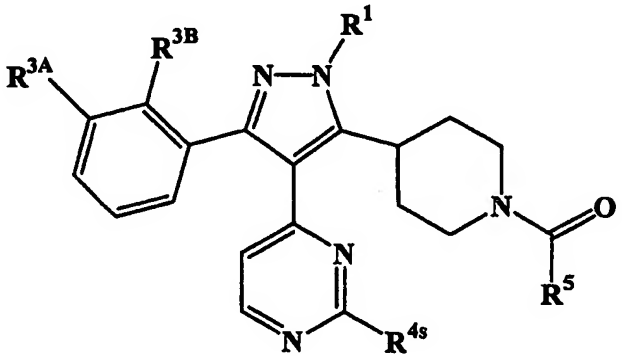
(48-4A).

In some embodiments, the preferred optical isomer of the compound of Formulas (48-5) corresponds in structure to the following formula:



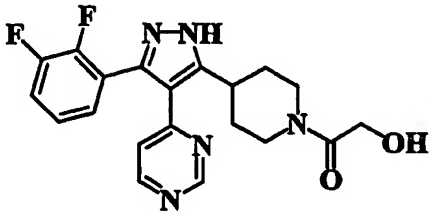
(48-5A).

[231] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

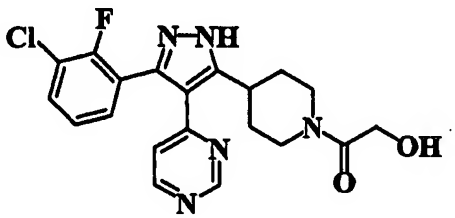


(49-1).

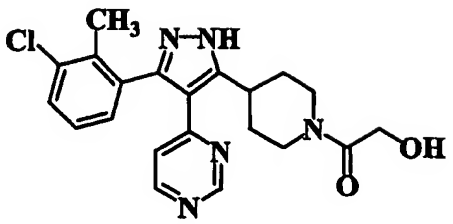
Examples of such compounds include those corresponding in structure to the following formulas:



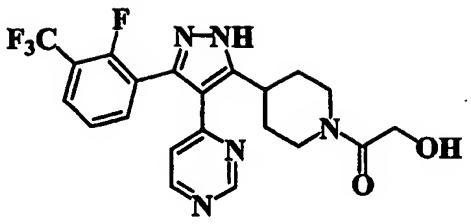
(50-1),



(50-2),

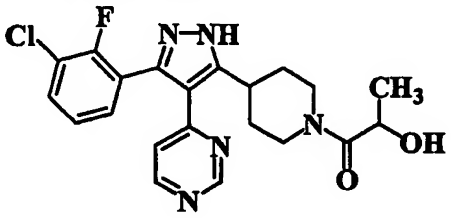


(50-3), and

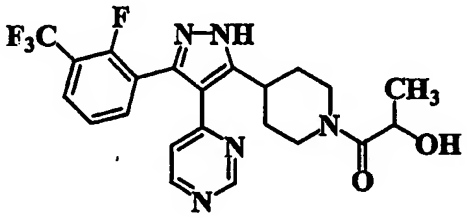


(50-4).

Other examples of such compounds include those corresponding in structure to the following formulas:

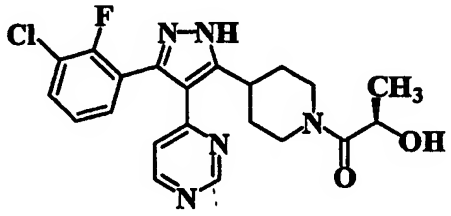


(50-5), and



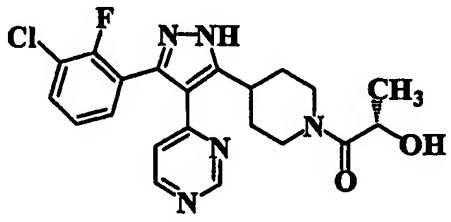
(50-6).

In some embodiments, the preferred optical isomer of the compound of Formula (50-5) corresponds in structure to the following formula:



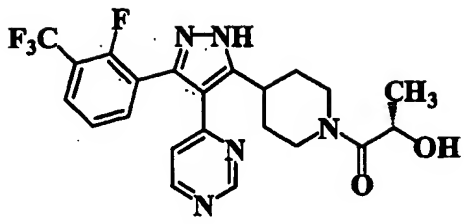
(50-5A).

In some embodiments, the preferred optical isomer of the compound of Formula (50-5) corresponds in structure to the following formula:



(50-5B).

In some embodiments, the preferred isomer of the compound of Formula (50-6) corresponds in structure to the following formula:



(50-6A).

Preferred Embodiment No. 2

[232] In some preferred embodiments:

[233] R^{3A} and R^{3B} are independently selected from the group consisting of halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, and alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, cycloalkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[234] R^4 is pyrimidinyl, maleimidyl, pyridonyl, pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino,

carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

Particularly Preferred Compounds of Embodiment No. 2

[235] In some particularly preferred embodiments, R^1 is hydrogen.

[236] In some particularly preferred embodiments, L^1 is a bond.

[237] In some particularly preferred embodiments, R^{3C} is hydrogen.

[238] In some particularly preferred embodiments, X^2, X^3, X^5, and X^6 are each $-CH_2-$.

[239] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, and alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[240] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of halogen, methyl, methoxy, halomethyl, and halomethoxy.

[241] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, fluoro, methyl, methoxy, chloromethyl, fluoromethyl, chloromethoxy, and fluoromethoxy.

[242] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, methyl, methoxy, chloromethyl, and chloromethoxy.

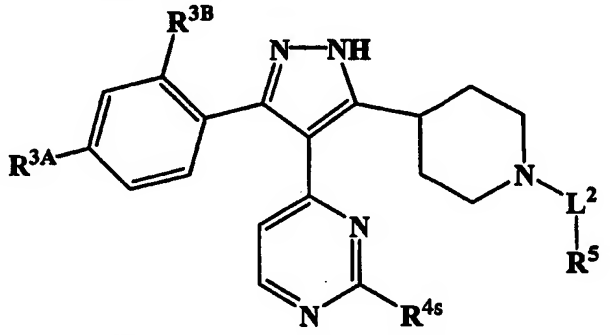
[243] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, methyl, methoxy, fluoromethyl, and fluoromethoxy.

[244] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, chloromethyl, and chloromethoxy.

[245] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, fluoromethyl, and fluoromethoxy.

In some particularly preferred embodiments, R^4 is pyrimidinyl substituted with alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent, in turn, is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[246] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(56-1).

In these embodiments, R^{4s} is alkyl, aminoalkyl, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, or alkylaminocarbonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[247] In some such embodiments, R^{4s} is alkoxycarbonyl, carbocyclyloxycarbonyl, or heterocyclyloxycarbonyl. Any such substituent optionally is

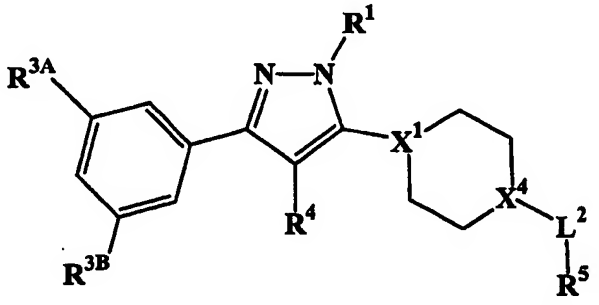
substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[248] In some other such embodiments, R^{4s} is alkylaminocarbonyl optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[249] In some other such embodiments, R^{4s} is $-CH_2OH$, $-C(CH_3)(H)-OH$, or $-C(CH_3)_2-OH$.

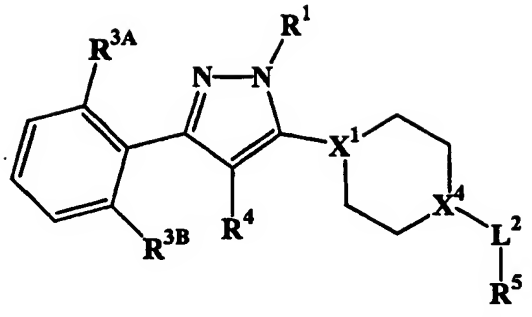
[250] In some other such embodiments, R^{4s} is aminomethyl. In these embodiments, the amino nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, haloalkyl, alkylsulfonyl, alkoxyalkyl, and heterocyclyl.

[251] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



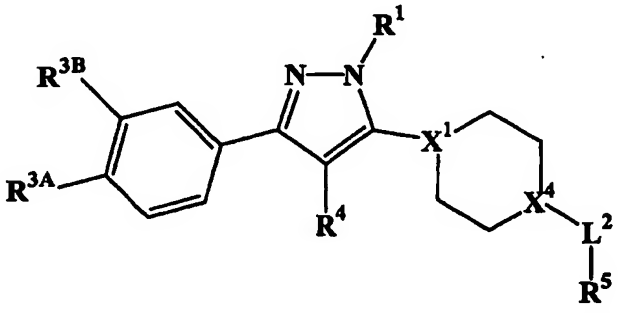
(62-1).

[252] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



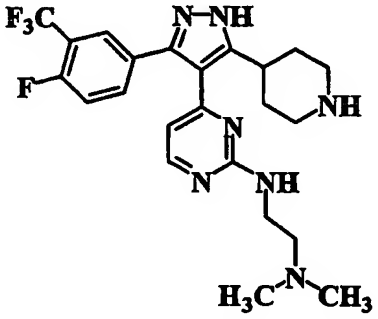
(63-1).

[253] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

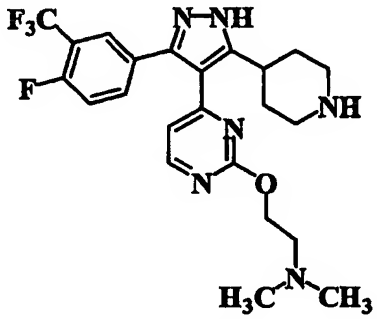


(64-1).

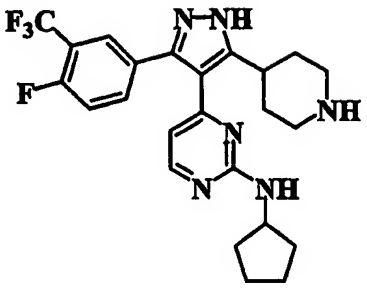
Examples of such compounds include, for example, those corresponding in structure to the following formulas:



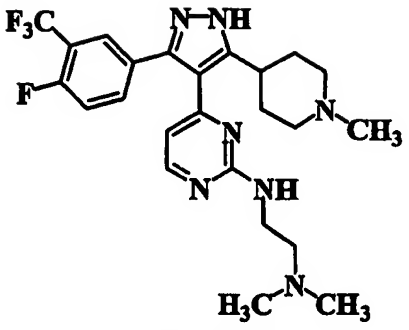
(65-1),



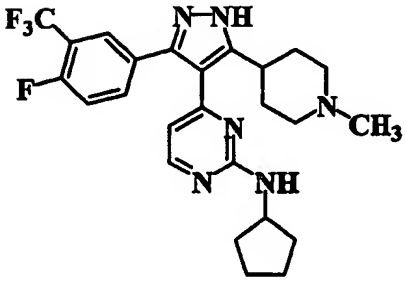
(65-2),



(65-3),

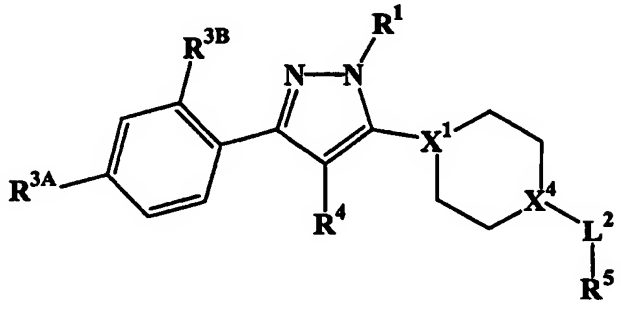


(65-4), and



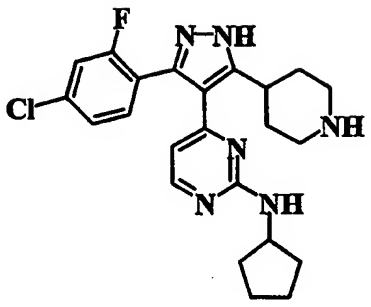
(65-5).

[254] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

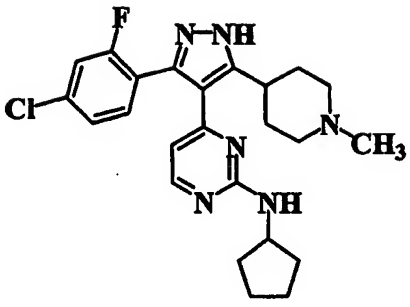


(66-1).

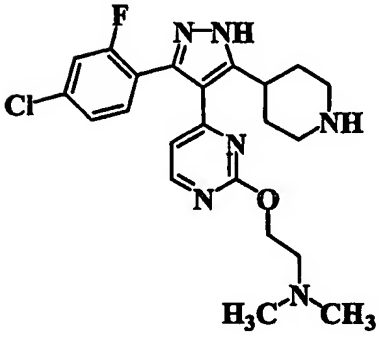
Examples of such compounds include, for example, those corresponding in structure to the following formulas:



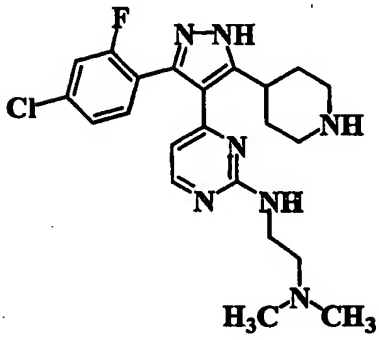
(67-1),



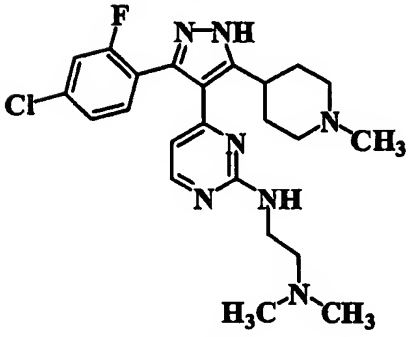
(67-2),



(67-3),

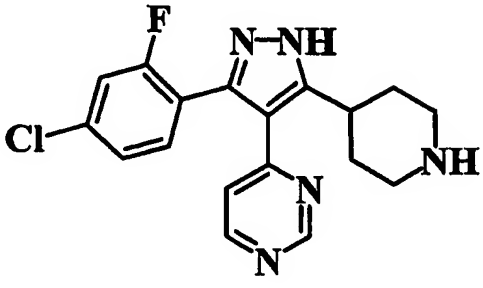


(67-4), and



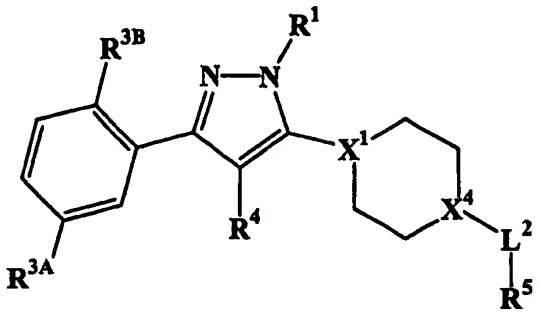
(67-5).

Another such compound, for example, corresponds in structure to the following formula:



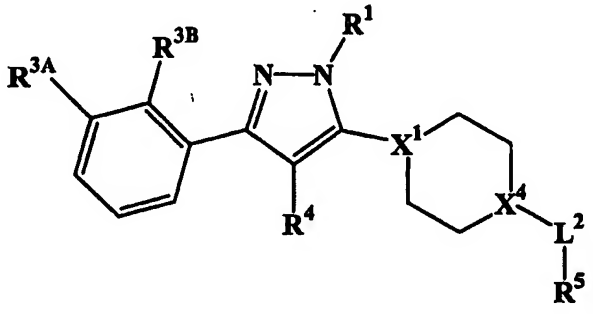
(67-6).

[255] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(68-1).

[256] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



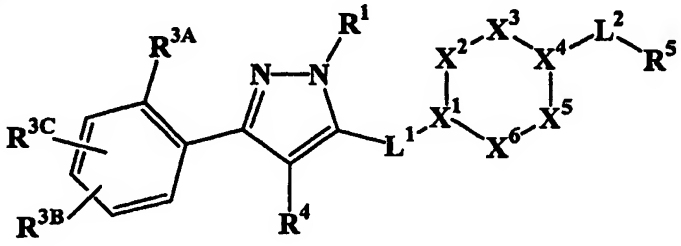
(69-1).

[257] In some particularly preferred embodiments, $-L^2-R^5$ is hydrogen, methyl, or butyloxycarbonyl.

[258] In some particularly preferred embodiments, $-L^2-R^5$ is hydrogen or alkyl.

Preferred Embodiment No. 3

[259] In some preferred embodiments, the compound corresponds in structure to the following formula:



(70-1).

Here, R^{3A} and R^{3B} are independently selected from the group consisting of halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, and

alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

Particularly Preferred Compounds of Embodiment No. 3

[260] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[261] In some particularly preferred embodiments, R^1 is hydrogen.

[262] In some particularly preferred embodiments, L^1 is a bond.

[263] In some particularly preferred embodiments, R^{3C} is hydrogen.

[264] In some particularly preferred embodiments, R^{3A} is halogen, methyl, methoxy, halomethyl, or halomethoxy.

[265] In some particularly preferred embodiments, R^{3A} is chloro, chloromethyl, or chloromethoxy.

[266] In some particularly preferred embodiments, R^{3A} is fluoro, fluoromethyl, or fluoromethoxy.

[267] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of halogen, methyl, methoxy, halomethyl, and halomethoxy.

[268] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, fluoro, methyl, methoxy, chloromethyl, fluoromethyl, chloromethoxy, and fluoromethoxy.

[269] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, methyl, methoxy, chloromethyl, and chloromethoxy.

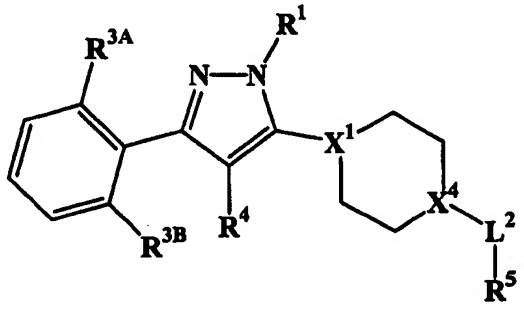
[270] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, methyl, methoxy, fluoromethyl, and fluoromethoxy.

[271] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of chloro, chloromethyl, and chloromethoxy.

[272] In some particularly preferred embodiments, R^{3A} and R^{3B} are independently selected from the group consisting of fluoro, fluoromethyl, and fluoromethoxy.

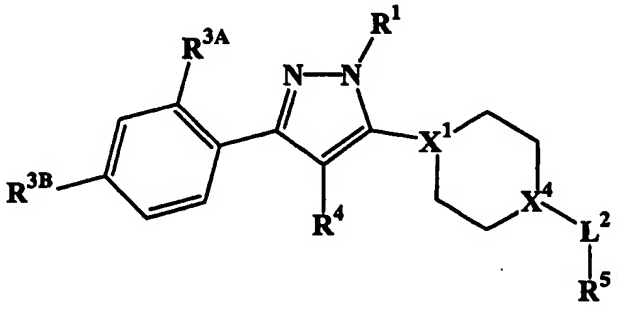
[273] In some particularly preferred embodiments, X^2, X^3, X^5, and X^6 are each $-CH_2-$.

[274] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



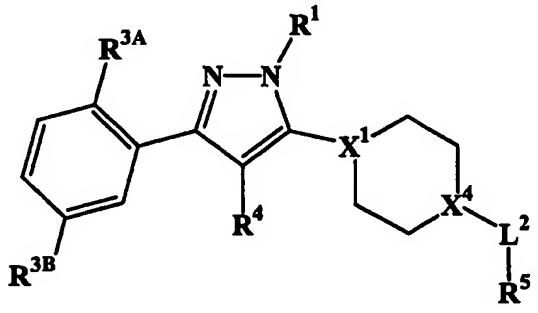
(72-1).

[275] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



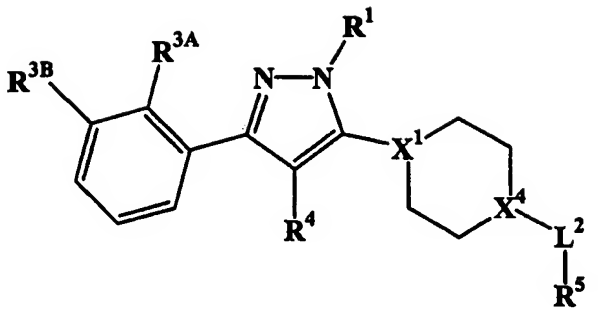
(73-1).

[276] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(74-1).

[277] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(75-1).

[278] In some particularly preferred embodiments, $-L^2-R^5$ is hydrogen, methyl, or butyloxycarbonyl.

Preferred Embodiment No. 4

[279] In some preferred embodiments:

[280] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[281] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[282] R^4 is pyridazinyl, pyrazinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio,

heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

Particularly Preferred Compounds of Embodiment No. 4

[283] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[284] In some particularly preferred embodiments, R^1 is hydrogen.

[285] In some particularly preferred embodiments, L^1 is a bond.

[286] In some particularly preferred embodiments, R^{3C} is hydrogen.

[287] In some particularly preferred embodiments, X^2, X^3, X^5, and X^6 are each $-CH_2-$.

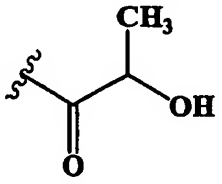
[288] In some particularly preferred embodiments, $-L^2$ is -C(O)-.

[289] In some particularly preferred embodiments, $-L^2$ is -O-.

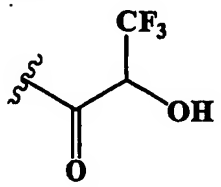
[290] In some particularly preferred embodiments, R^5 is alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, or tetrahydrofuranylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy and halogen.

[291] In some particularly preferred embodiments, R^5 is hydrogen, alkenyl, or alkylcarbonylalkyl.

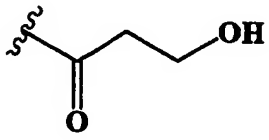
[292] In some particularly preferred embodiments, $-L^2-R^5$ corresponds in structure to one of the following formulas:



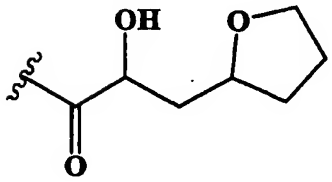
(81-1),



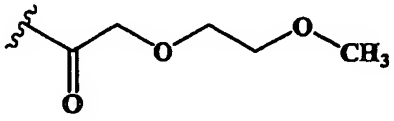
(81-2),



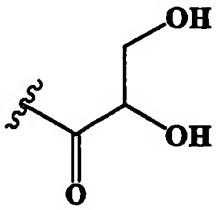
(81-3),



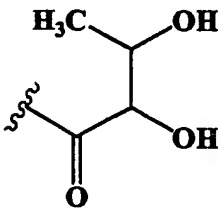
(81-4),



(81-5),



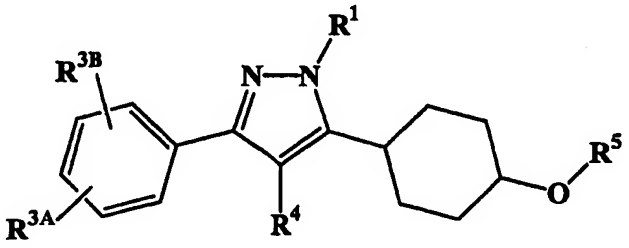
(81-6), and



(81-7).

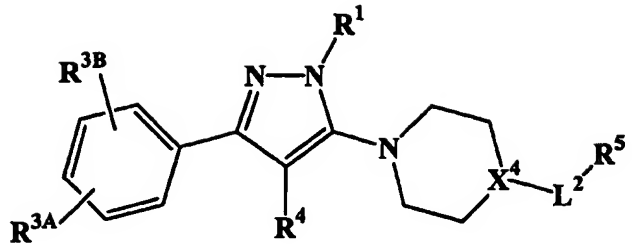
[293] In some particularly preferred embodiments, $-L^2-R^5$ is alkylcarbonyl substituted with one or more hydroxy.

[294] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



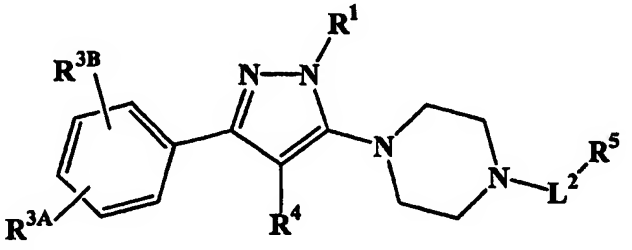
(83-1).

[295] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



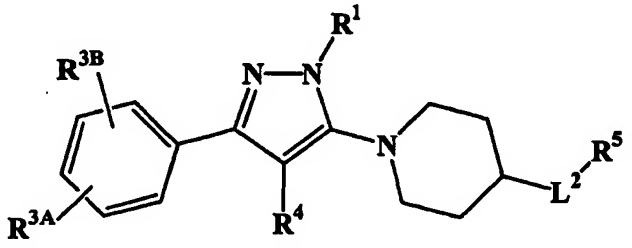
(85-1).

[296] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



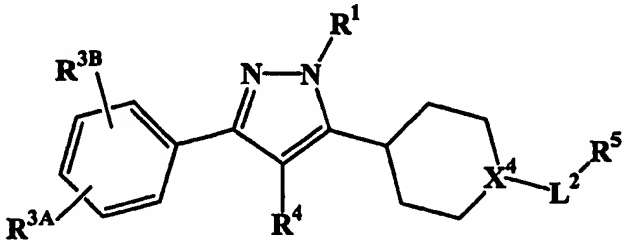
(86-1).

[297] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



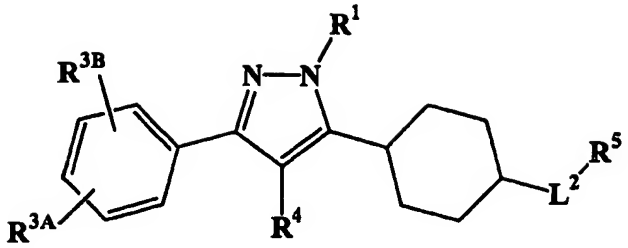
(87-1).

[298] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(88-1).

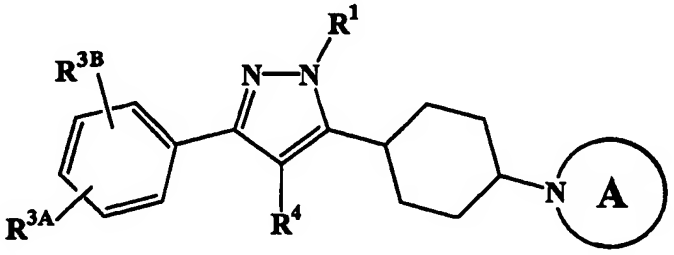
[299] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(89-1).

[300] In some particularly preferred embodiments, L^2 is a bond; and R^5 is heterocyclyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[301] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

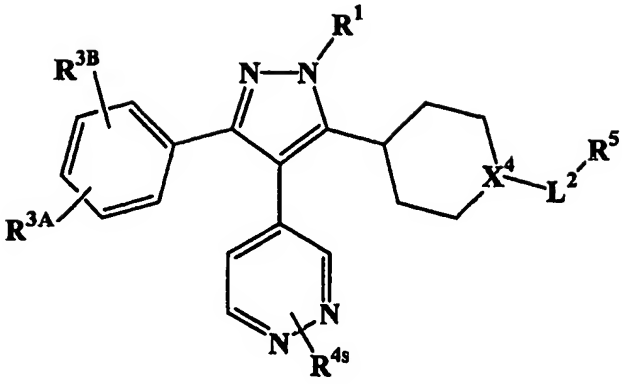


(91-1).

Here, the ring structure A is a heterocyclyl ring containing a nitrogen bonded to the cyclohexyl. The heterocyclyl ring also is optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

[302] In some particularly preferred embodiments, L^2 is $-N(R^a)-$; and R^5 is alkyl, carbocyclyl, or carbocyclylalkyl. The alkyl, carbocyclyl, or carbocyclylalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

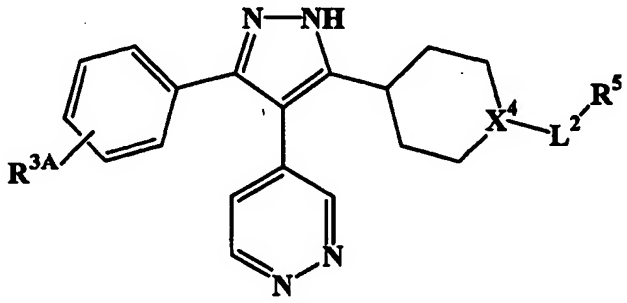
[303] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(93-1).

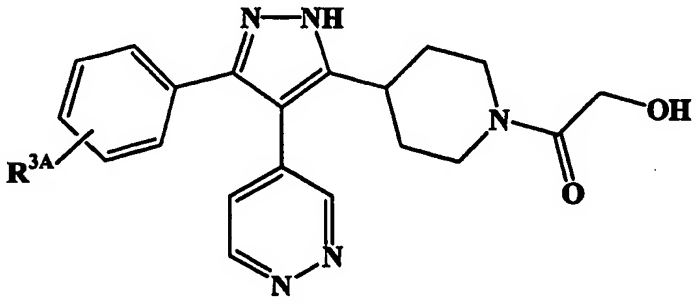
[304] In some such particularly preferred embodiments, R^{4s} is hydrogen, alkylthio, mono-alkylamino, di-alkylamino, alkoxy, or haloalkoxy.

[305] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



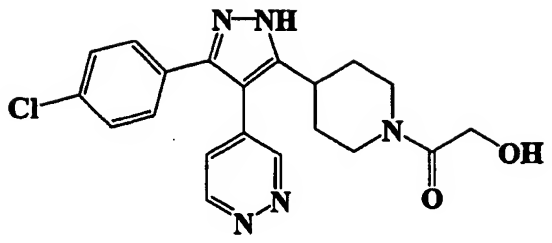
(95-1).

In some such embodiments, the compound corresponds in structure to the following formula:



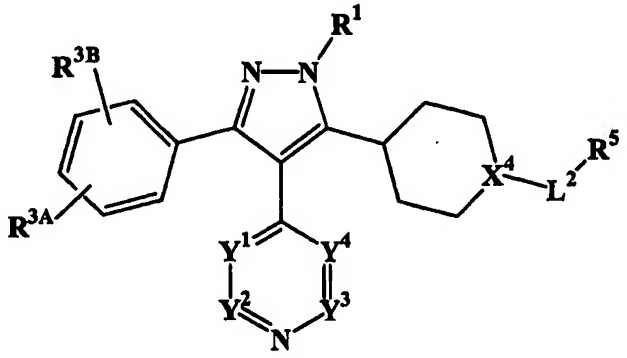
(97-1).

One such compound, for example, corresponds in structure to the following formula:



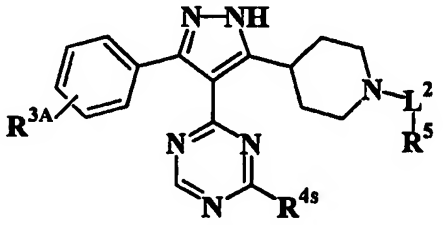
(98-1).

[306] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

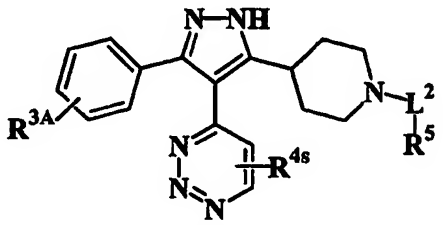


(99-1).

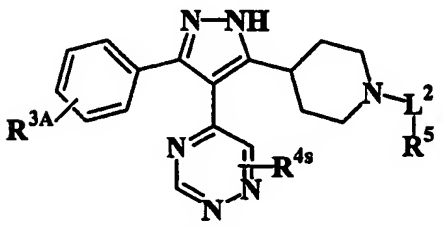
Here, two of Y^1, Y^2, Y^3, and Y^4 are each nitrogen, one of Y^1, Y^2, Y^3, and Y^4 is carbon bonded to R^{4s}, and one of Y^1, Y^2, Y^3, and Y^4 is carbon bonded to hydrogen. In some such embodiments, the compound corresponds in structure to one of the following formulas:



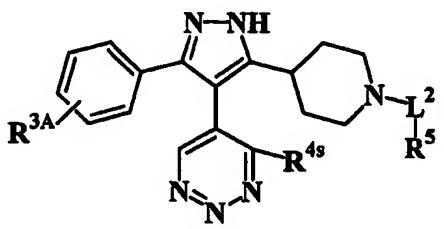
(100-1),



(100-2),

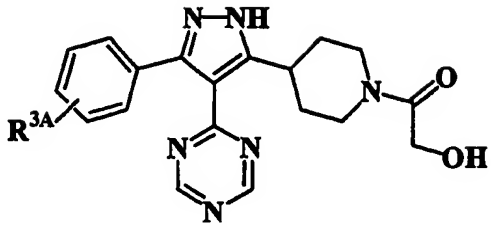


(100-3), and

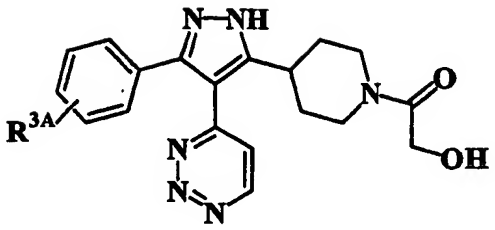


(100-4).

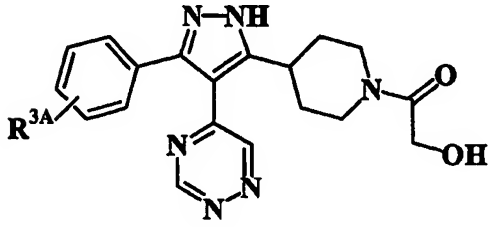
In such embodiments, for example, the compound corresponds in structure to one of the following formulas:



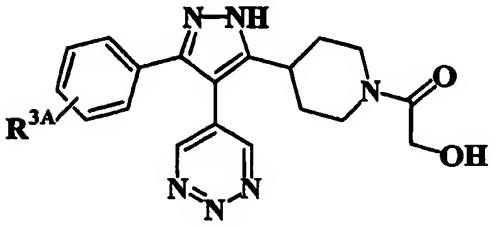
(102-1),



(102-2),

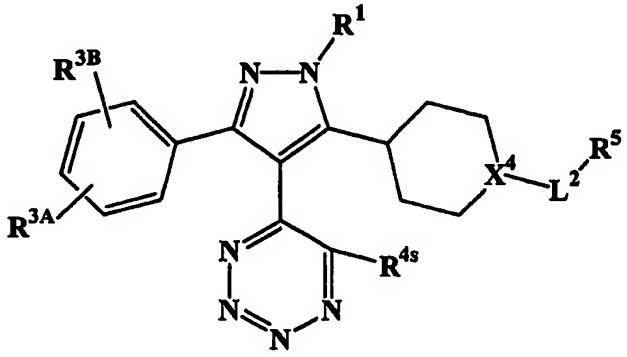


(102-3), and



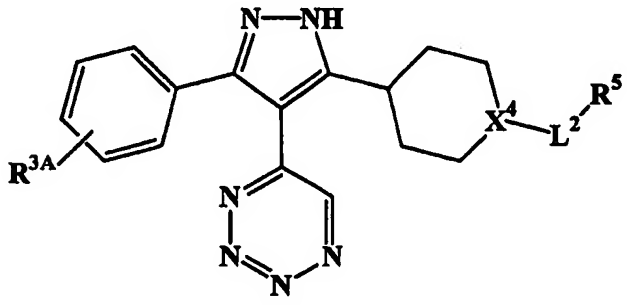
(102-4).

[307] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



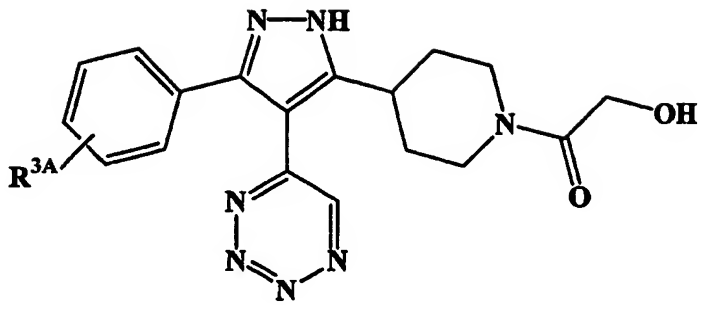
(103-1).

In some such embodiments, the compound corresponds in structure to the following formula:



(104-1).

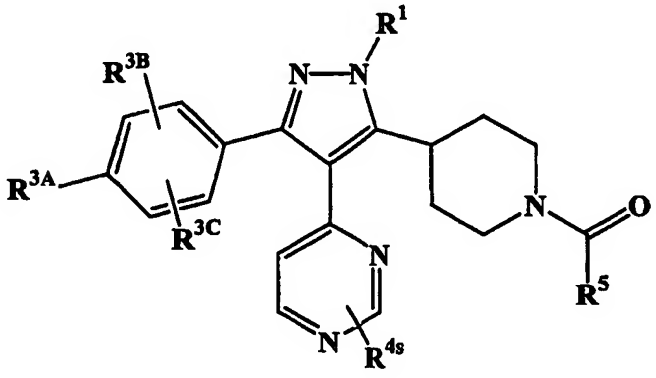
These embodiments include, for example, compounds corresponding in structure to the following formula:



(106-1).

Preferred Embodiment No. 5

[308] In some preferred embodiments, the compound corresponds in structure to the following formula:



(107-1).

Here:

[309] R^{3A} is hydroxy, cyano, amino, monomethylamino, monoethylamino, dimethylamino, diethylamino, N-methyl-N-ethyl-amino, methyl, ethyl, haloethyl, propyl, halopropyl, aminomethyl, aminoethyl, hydroxymethyl, hydroxyethyl, methoxy, ethoxy, haloethoxy, methoxymethyl, or halomethoxymethyl.

[310] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[311] R^5 is hydroxyalkyl.

Particularly Preferred Compounds of Embodiment No. 5

[312] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[313] In some particularly preferred embodiments, R^1 is hydrogen.

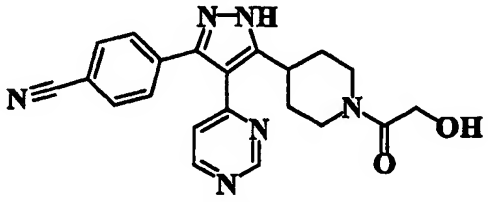
[314] In some particularly preferred embodiments, R^{3C} is hydrogen.

[315] In some particularly preferred embodiments, R^{4s} is hydrogen.

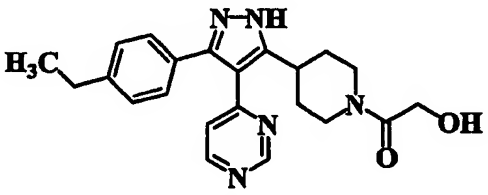
[316] In some particularly preferred embodiments, R^5 is C_1-C_6-hydroxyalkyl.

[317] In some particularly preferred embodiments, R^5 is hydroxymethyl.

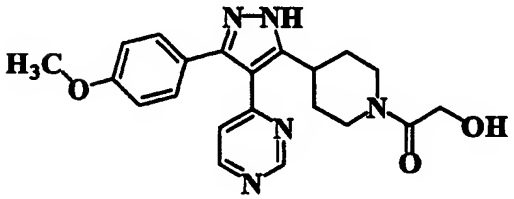
Examples of such compounds include, for example, those corresponding in structure to the following formulas:



(109-1),



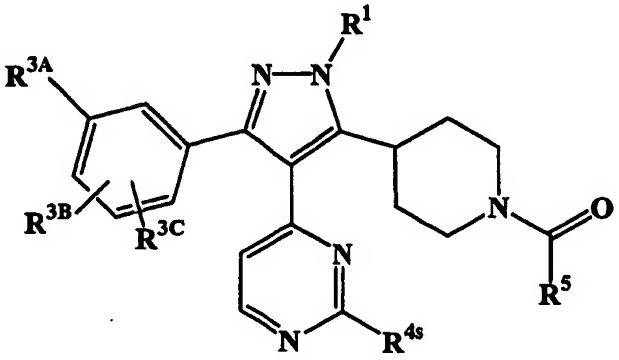
(109-2), and



(109-3).

Preferred Embodiment No. 6

[318] In some preferred embodiments, the compound corresponds in structure to the following formula:



(110-1).

Here:

[319] R^{3A} is hydroxy, cyano, amino, monomethylamino, monoethylamino, dimethylamino, diethylamino, N-methyl-N-ethyl-amino, methyl, ethyl, haloethyl, propyl, halopropyl, aminomethyl, aminoethyl, hydroxymethyl, hydroxyethyl, methoxy, halomethoxy, ethoxy, haloethoxy, methoxymethyl, or halomethoxymethyl.

[320] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[321] R^5 is hydroxyalkyl.

Particularly Preferred Compounds of Embodiment No. 6

[322] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[323] In some particularly preferred embodiments, R^1 is hydrogen.

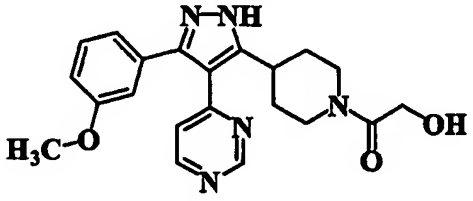
[324] In some particularly preferred embodiments, R^{3C} is hydrogen.

[325] In some particularly preferred embodiments, R^{4s} is hydrogen.

[326] In some particularly preferred embodiments, R^5 is C_1-C_6-hydroxyalkyl.

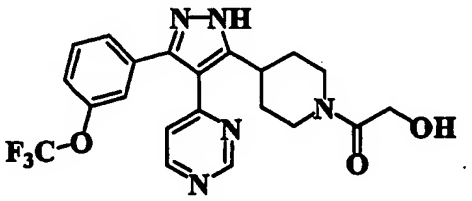
[327] In some particularly preferred embodiments, R^5 is hydroxymethyl.

[328] Examples of particularly preferred compounds include those corresponding in structure to the following formulas:



(112-1)

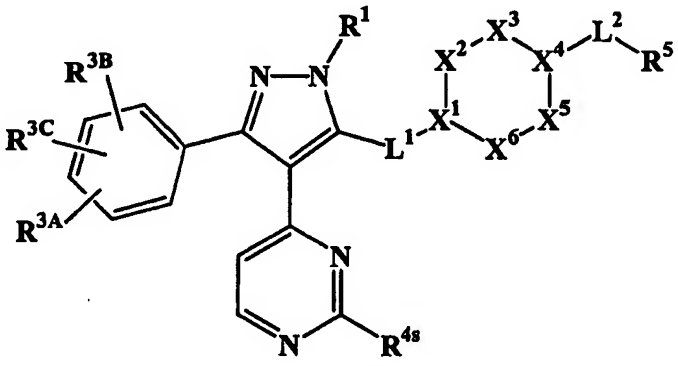
and



(112-2).

Preferred Embodiment No. 7

[329] In some preferred embodiments, the compound corresponds in structure to the following formula:



(113-1).

Here:

[330] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[331] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[332] R^5 is phosphonooxyalkyl, monoalkylphosphonooxyalkyl, dialkylphosphonooxyalkyl, aminoalkylcarbonyloxyalkyl, monoalkylaminoalkylcarbonyloxyalkyl, dialkylaminoalkylcarbonyloxyalkyl, phenylalkyl substituted with alkylcarbonyloxy, or tetrahydrofuranyl.

Particularly Preferred Compounds of Embodiment No. 7

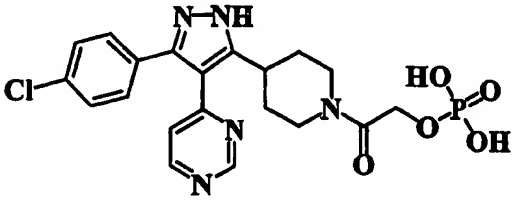
[333] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[334] In some particularly preferred embodiments, R^1 is hydrogen.

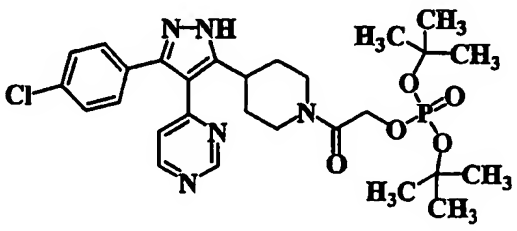
[335] In some particularly preferred embodiments, R^{3C} is hydrogen.

[336] In some particularly preferred embodiments, R^{48} is hydrogen.

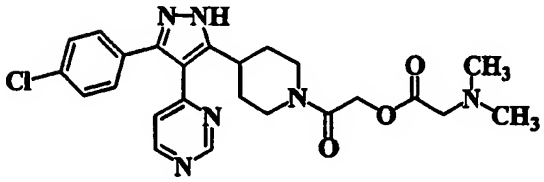
[337] Examples of particularly preferred compounds include those corresponding in structure to the following formulas:



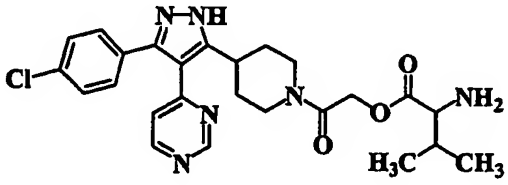
(114-1),



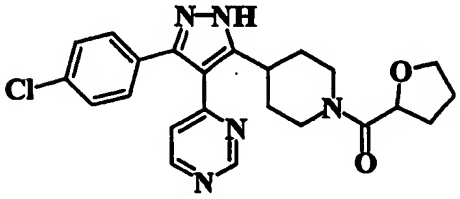
(114-2),



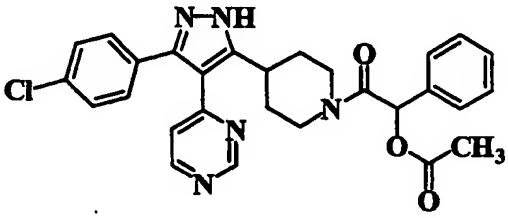
(114-3),



(114-4),

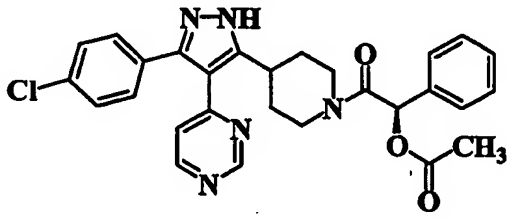


(114-5), and



(114-6).

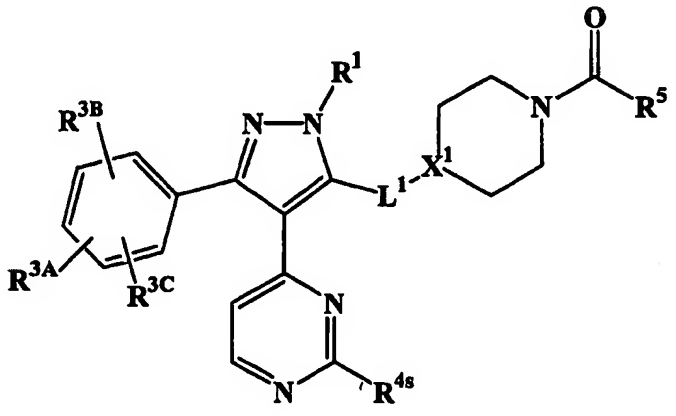
In some embodiments, the preferred optical isomer of the compound of Formula (114-6) corresponds in structure to the following formula:



(114-6A).

Preferred Embodiment No. 8

[338] In some preferred embodiments, the compound corresponds in structure to the following formula:



(115-1).

Here:

[339] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[340] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[341] R^{4s} is hydrogen, alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, arylalkyl, hetercycloalkylalkyl, heteroarylalkyl, amino, alkylamino, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, arylamino, heterocycloalkylamino, heteroarylamino, hydroxy, alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, aryloxy, heterocycloalkyloxy, heteroaryloxy, thiol, alkylthio, cycloalkylthio, arylthio, heterocycloalkylthio, heteroarylthio, aminosulfonyl, alkylsulfonyl, cycloalkylsulfonyl, arylsulfonyl, heterocycloalkylsulfonyl, or heteroarylsulfonyl. Any such substituent

optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy, cyano, and alkyl.

[342] R^5 is alkylcarbonyloxyalkyl.

Particularly Preferred Compounds of Embodiment No. 8

[343] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[344] In some particularly preferred embodiments, R^1 is hydrogen.

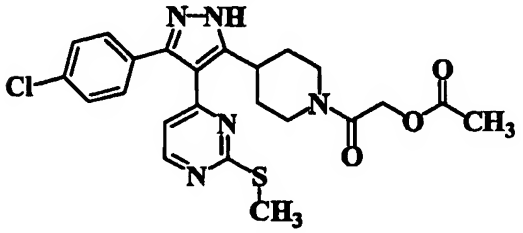
[345] In some particularly preferred embodiments, R^{3C} is hydrogen.

[346] In some particularly preferred embodiments, R^{4s} is hydrogen.

[347] In some particularly preferred embodiments, X^1 is carbon bonded to hydrogen.

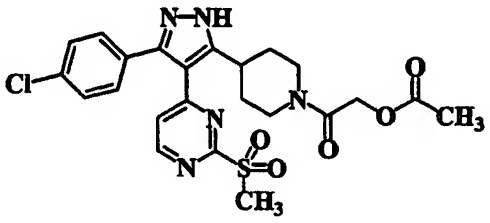
[348] In some particularly preferred embodiments, L^1 is a bond.

[349] In some particularly preferred embodiments, R^5 is methylcarbonyloxymethyl. Examples of such compounds include those corresponding in structure to the following formulas:



(119-1)

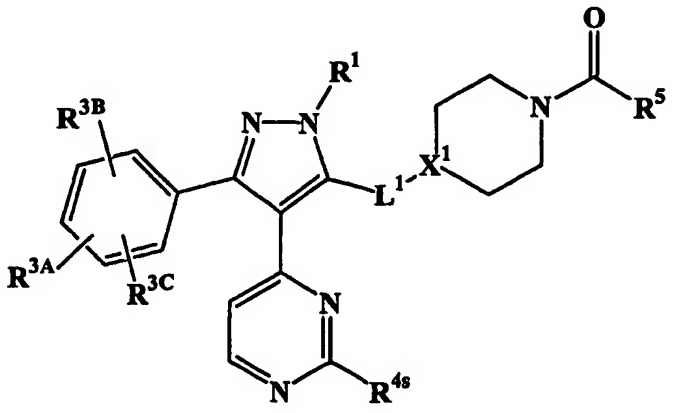
and



(119-2).

Preferred Embodiment No. 9

[350] In some preferred embodiments, the compound corresponds in structure to the following formula:



(120-1).

Here:

[351] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[352] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[353] R^{4s} is hydrogen, C_1-C_6-alkyl, aminoalkyl, alkoxyalkyl, cycloalkylalkyl, hetercycloalkylalkyl, heteroarylalkyl, aminoalkylamino, alkoxyalkylamino, cycloalkylamino, heterocycloalkylamino, heteroarylamino, hydroxy, C_2-C_6-alkoxy, aminoalkoxy, alkoxyalkoxy, cycloalkyloxy, heterocycloalkyloxy, heteroaryloxy, thiol, C_2-C_6-alkylthio, cycloalkylthio, heterocycloalkylthio, heteroarylthio, aminosulfonyl, C_2-C_6-alkylsulfonyl, cycloalkylsulfonyl, heterocycloalkylsulfonyl, or heteroarylsulfonyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of hydroxy, cyano, and alkyl.

[354] R^5 is hydroxyalkyl.

Particularly Preferred Compounds of Embodiment No. 9

[355] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

[356] In some particularly preferred embodiments, R^1 is hydrogen.

[357] In some particularly preferred embodiments, R^{3C} is hydrogen.

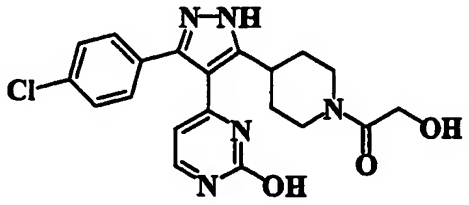
[358] In some particularly preferred embodiments, R^{4s} is hydrogen.

[359] In some particularly preferred embodiments, X^1 is carbon bonded to hydrogen.

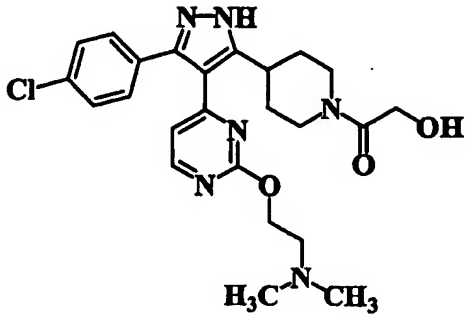
[360] In some particularly preferred embodiments, L^1 is a bond.

[361] In some particularly preferred embodiments, R^5 is hydroxymethyl.

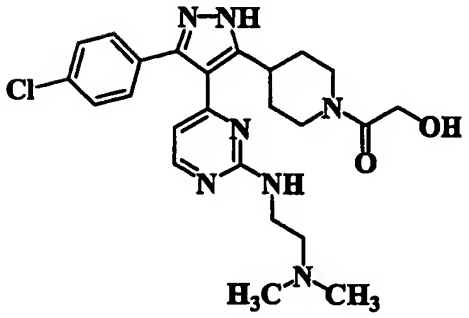
Examples of such compounds include those corresponding in structure to the following formulas:



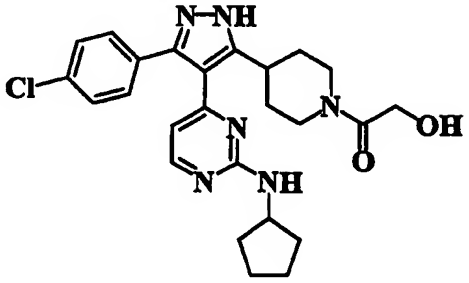
(124-1),



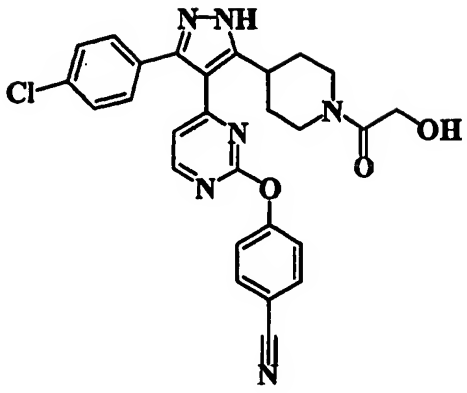
(124-2),



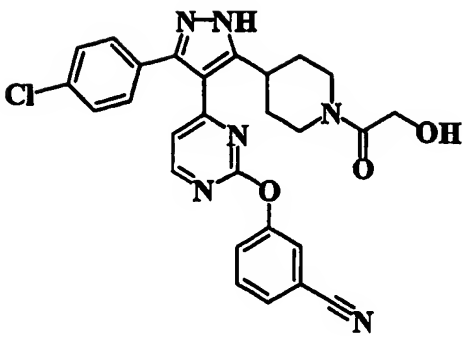
(124-3),



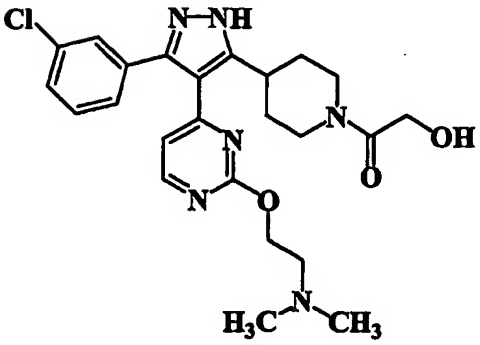
(124-4),



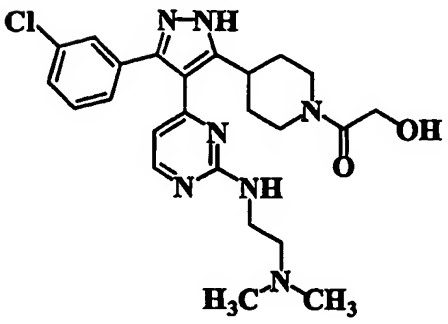
(124-5),



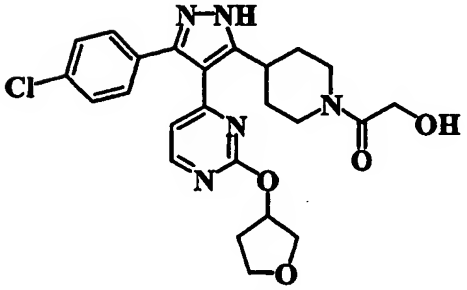
(124-6),



(124-7),

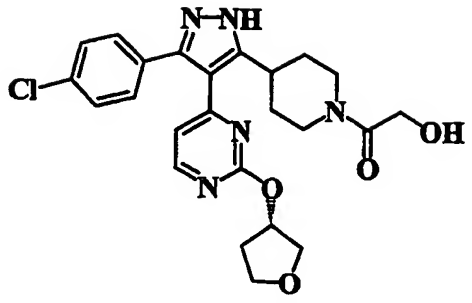


(124-8), and



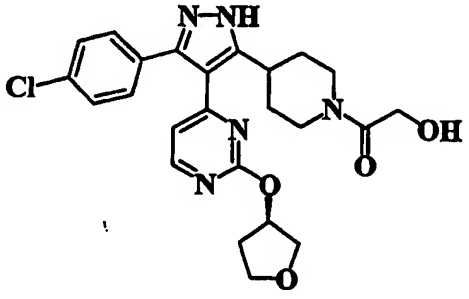
(124-9).

In some embodiments, the preferred optical isomer of the compound of Formula (124-9) corresponds in structure to the following formula:



(124-9A).

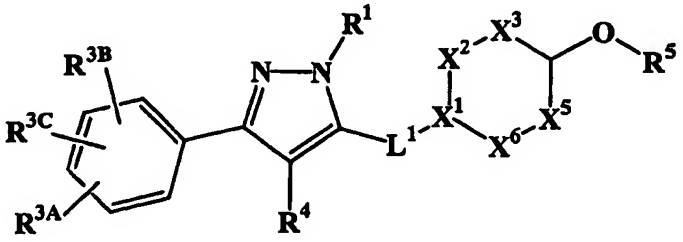
In some embodiments, the preferred optical isomer of the compound of Formula (124-9) corresponds in structure to the following formula:



(124-9B).

Preferred Embodiment No. 10

[362] In some preferred embodiments, the compound corresponds in structure to the following formula:



(125-1).

Here,

[363] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[364] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[365] R^4 is pyridazinyl, pyrazinyl, pyrimidinyl, triazinyl, tetrazinyl, benzazinyl, benzodiazinyl, naphthyridinyl, pyridopyridinyl, pyrinyl, maleimidyl, pyridonyl, thiazolyl, isothiazolyl, thiazolylalkyl, isothiazolylalkyl, thiazolylamino, isothiazolylamino, thiomorpholinyl, the sulfoxide of thiomorpholinyl, or the sulfone of thiomorpholinyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl. Any such optional substituent is, in turn, optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[366] R^5 is hydrogen, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

Particularly Preferred Compounds of Embodiment No. 10

[367] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

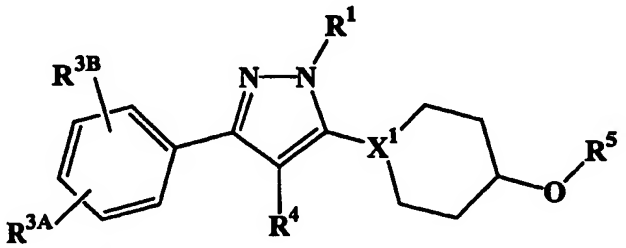
[368] In some particularly preferred embodiments, R^1 is hydrogen.

[369] In some particularly preferred embodiments, R^{3C} is hydrogen.

[370] In some particularly preferred embodiments, X^1 is carbon bonded to hydrogen.

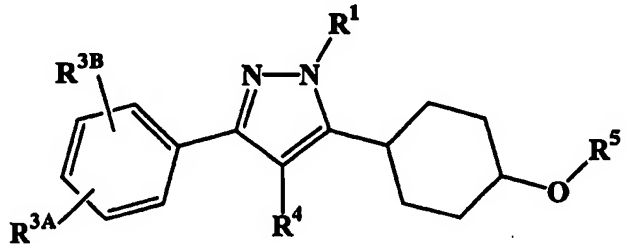
[371] In some particularly preferred embodiments, L^1 is a bond.

[372] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



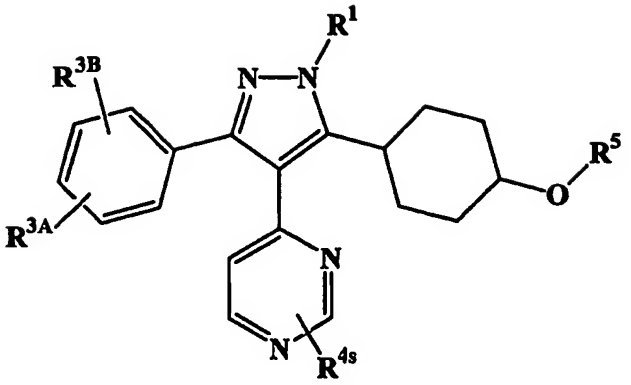
(126-1).

[373] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



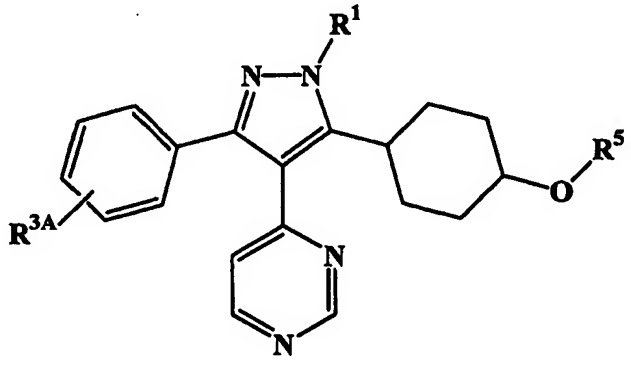
(127-1).

[374] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(128-1).

[375] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:

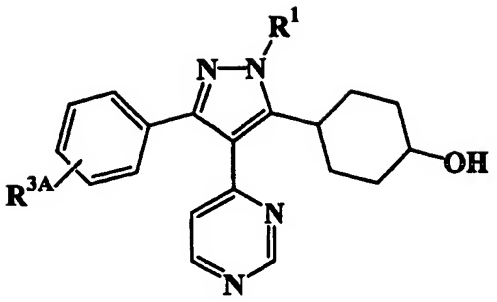


(129-1).

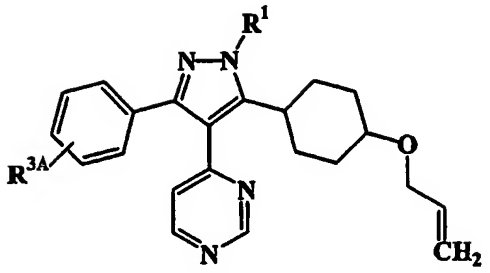
[376] In some particularly preferred embodiments, R^5 is hydrogen, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl.

[377] In some particularly preferred embodiments, R^5 is hydrogen, alkenyl, or alkylcarbonylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkoxy, and haloalkoxy.

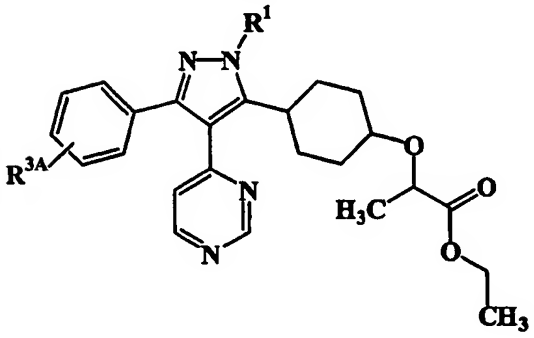
[378] In some particularly preferred embodiments, the compound corresponds in structure to one of the following formulas:



(132-1),

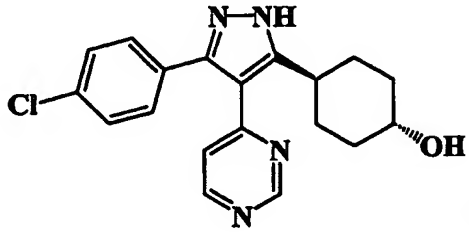


(132-2), and



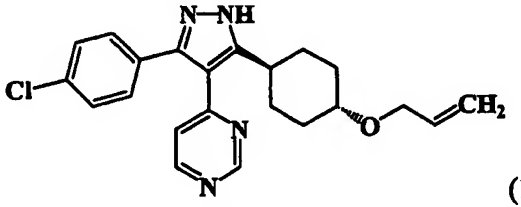
(132-3).

In some embodiments, the preferred isomer of the compound of Formula (132-1) corresponds in structure to the following formula:



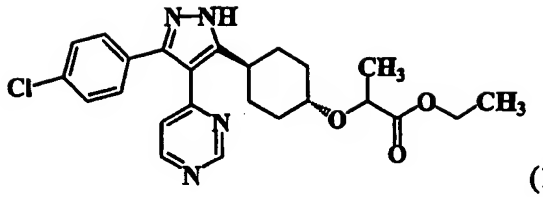
(132-1A).

In some embodiments, the preferred isomer of the compound of Formula (132-2) corresponds in structure to the following formula:



(132-2A).

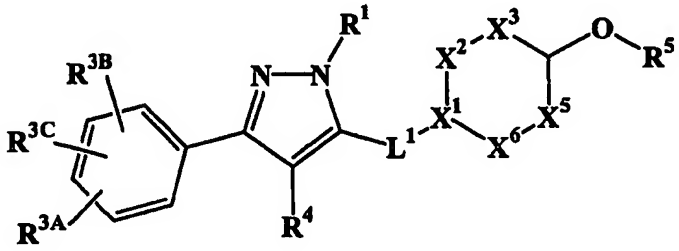
In some embodiments, the preferred isomer of the compound of Formula (132-3) corresponds in structure to the following formula:



(132-3A).

Preferred Embodiment No. 11

[379] In some preferred embodiments, the compound corresponds in structure to the following formula:



(133-1).

Here:

[380] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[381] R^{3B} is hydrogen, halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and cyano.

[382] R^4 is pyridinyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, thiol, carboxy, nitro, alkyl, carboxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclyloxy, carbocyclylalkoxy, carbocyclyloxyalkyl, carbocyclylthio, carbocyclylsulfinyl, carbocyclylsulfonyl, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, carbocyclylalkoxy, carbocyclylheterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylalkoxy, amino,

aminoalkyl, alkylamino, alkenylamino, alkynylamino, carbocyclylamino, heterocyclylamino, aminocarbonyl, alkoxy, alkoxyalkyl, alkenyloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, carbocyclyloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxycarbocyclylamino, alkoxycarbocyclylalkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkoxyalkoxy, aminoalkoxy, aminoalkylamino, alkylaminoalkylamino, carbocyclylalkylamino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, carbocyclylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, alkylaminocarbonyl, alkylcarbonylamino, hydrazinyl, alkylhydrazinyl, and carbocyclylhydrazinyl. Any such optional substituent optionally is substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halogen, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkoxy.

[383] R^5 is alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylcarbonylalkyl, alkoxycarbonylalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, or heterocyclylalkyl. Any such substituent optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, alkyl, haloalkyl, hydroxyalkyl, alkoxy, and haloalkoxy.

Particularly Preferred Compounds of Embodiment No. 11

[384] In some particularly preferred embodiments, R^1 is hydroxyalkyl.

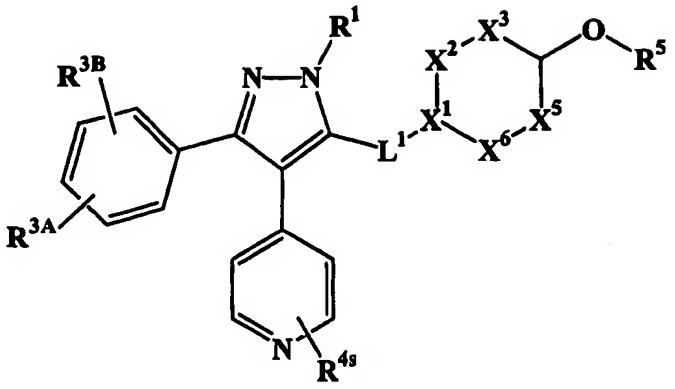
[385] In some particularly preferred embodiments, R^1 is hydrogen.

[386] In some particularly preferred embodiments, R^{3C} is hydrogen.

[387] In some particularly preferred embodiments, X^1 is carbon bonded to hydrogen.

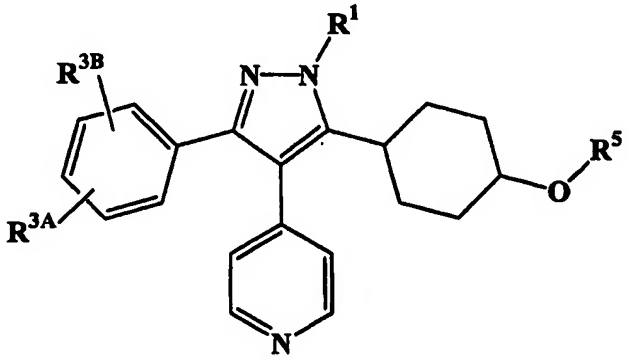
[388] In some particularly preferred embodiments, L^1 is a bond.

[389] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(134-1).

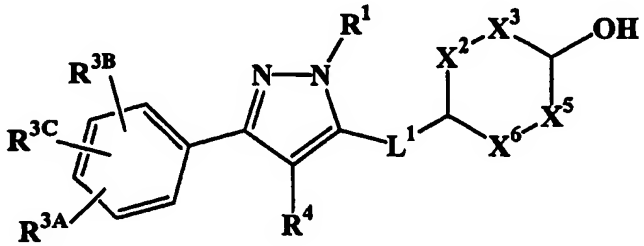
[390] In some particularly preferred embodiments, the compound corresponds in structure to the following formula:



(135-1).

Preferred Embodiment No. 12

[391] In some preferred embodiments, the compound corresponds in structure to the following formula:



(136-1).

Here:

[392] R^{3A} is halogen, hydroxy, cyano, amino, alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl. Any carbon of the alkyl, aminoalkyl, monoalkylamino, dialkylamino, alkoxy, or alkoxyalkyl optionally is